AN EXAMINATION OF A NOVEL WEIGHT LOSS FORMULA ON ANTHROPOMETRY AND INDICES OF CARDIOVASCULAR DISEASE RISK

A Dissertation

by

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ABSTRACT

Studies from Africa report supplementation with *Dichrostachys glomerata* (DG; 200–400 mg/d) has led to significant reductions in weight and fat in obese individuals, without exercise or diet intervention. The purpose of this study was to examine if adding DG to weight loss supplements with caffeine [WL+C] containing; DG (300mg), Clubmoss extract (10mg), Caffeine (150mg; XR [77% caffeine] | 250mg; anhydrous [98.5% caffeine]), Sensoril® (125mg), and Capsimax® (50mg) or without caffeine [WL] containing; DG (300mg), Sensoril® (250mg; Ashwaganda), Bioperine (5mg), Capsimax® (50mg; 4% Capsaicinoids), Rhodiola rosea extract (60mg), L-Theanine (100mg), Clubmoss extract (5mg), and Bacopa monneri extract (50mg), would promote weight loss in overweight persons, without exercise or dietary modification. In a double-blind, parallel, stratified random, placebo-controlled trial, participants (N=68 [M: 31, W: 37], 37±5 yr, 88.9±16.6 kg, BMI: 25-34.9 kg/m^2, Fat: 35.2±7.7%, Activity: 6,857±1,512 steps/wk) ingested a DG containing weight loss supplement for 12 weeks. Measurements were obtained for body weight, body composition, anthropometry, blood chemistries, resting energy expenditure, and hunger and satiety at baseline and after 4, 8, and 12-weeks. Supplementation was shown, using GLM, to have no significant differences between groups for measures of body composition using the current dose. Supplement groups decreased in FM (WL: -0.56±0.95 [-1.02, -0.14]; WL: -0.63±1.47 [-1.23, -0.02] kg) at wk4 and wk8, respectively, and body fat (WL: -0.63±1.26 [-1.16, -0.10]; WL: -0.78±1.31 [-1.45, 0.07] %) at wk8 and wk12, respectively, with indications of having greater effect

on males. As well, REE improved (WL+C: 111±220 [10, 207] kcal/d; WL+C: 1.57±2.37 [0.5, 2.6] kcal/kg/d) by wk12. Supplement groups also reported less hunger and more satiety with some sleep quality improvements (diminished sleep quality for WL+C), overall. No significant effects or differences were observed in any other measure. The addition of caffeine did not incur additional benefits. Consequently, further research is required to determine an effective dose and thereafter, paired with a diet and/or exercise program for functional assessment of weight loss potential.

DEDICATION

To my loving wife, Jennifer, and son, Oliver, thank you for carrying me through everything and giving my life purpose. I love you more than the English language can express; you are my Ikigai (生き甲斐).

As well to my mother-in-law, Robin, for all of your help, love, and support with both school and family. I literally could not have done this without you.

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Contributors

This work was supervised by a dissertation committee consisting of Dr. Richard Kreider [Chair of Committee], Dr. James Fluckey [Committee Member], and Dr. Steven Riechman [Committee Member] of the Department of Health and Kinesiology and Dr. Karen Kubena [Committee Member] of the Department of Nutrition and Food Science.

Ryan Sowinski served as study coordinator and assisted with data collection, sample analysis, data analysis, and manuscript preparation. Ryan Dalton, Tyler Grubic, Blaise Collins, Brittany Sanchez, Aimee Reyes, Adriana Coletta, Majid Koozehchain, and Peter Jung assisted in data collection and sample analysis. Christopher Rasmussen serves as coordinator of the Exercise and Sport Nutrition Lab and project manager. Dr. Mike Greenwood assisted in research design and consultation. Dr. Peter Murano served as quality assurance manager. Dr. Conrad Earnest served as scientific liaison to the sponsor and assisted in study design, data analysis, and interpretation. However, Dr. Conrad Earnest was not involved in data collection or data entry and there were no restrictions on publication of the data or preparation of this paper. Dr. Richard Kreider obtained the grant, served as study PI, and assisted in the design of the study, data analysis, and manuscript preparation.

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NOMENCLATURE

WL+C	Supplement formula with caffeine
WL	Supplement formula without caffeine
PLA	Placebo group (6 grams of dextrose)
FAM	Familiarization Session
CHO	Carbohydrates
PRO	Protein
kcal(s)	kilocalorie(s) (1 Calorie = 1 kcal = 1,000 calories)
~ or ≈	Approximately equal to
e.g.	*Exempli gratia*; “for sake of example”; for example
i.e	*Id est*; “that is”; in other words
ea	Each
g	Gram
kg	Kilogram
mg	Milligram
km	Kilometer
L	Liter
mL	Milliliter
kg/m^2	Kilogram per square meter
mRs	Milliradian
mmol	Millimole
min	Minute(s)

wk(s)	Week(s)
/d	per day
BID	Twice a day
/wk	per week
mo	Month(s)
yr(s)	Year(s)
y/o	Years old
w/o	Without
CI	Confidence Interval
AE	Adverse Events
NSAID	Non-Steroidal Anti-inflammatory Drug
T2DM	Type-2 Diabetes Mellitus
O_2	Oxygen
CO_2	Carbon Dioxide
VO_2	Oxygen consumption
VCO_2	Carbon Dioxide production
REE	Resting Energy Expenditure
HR	Heart Rate
BP	Blood Pressure
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
BMI	Body Mass Index

DEXA	Dual-Energy X-Ray Absorptiometry
FM	Fat Mass
FFM	Fat-Free Mass
BMC	Bone Mineral Content
BIA	Bioelectrical Impedance Analysis
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
ALP	Alkaline Phosphatase
BUN	Blood Urea Nitrogen
CRE	Creatinine
CK	Creatine Kinase
LDH	Lactate Dehydrogenase
LDL	Low Density Lipoprotein (Cholesterol)
HDL	High Density Lipoprotein (Cholesterol)
TRIG	Triglycerides
RBC	Red Blood Cells
RDW	Red Blood Cell Distribution Width
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MPV	Mean Platelet Volume
WBC	White Blood Cells

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CHAPTER I

INTRODUCTION AND RATIONALE

Background

In 2016, the World Health Organization (WHO)[1] placed the global prevalence of obesity (BMI ≥ 30 kg/m^2) and overweight (BMI ≥ 25 kg/m^2) adults (≥18 y/o) at 13% (650 million) and 39% (1.9 billion), respectively. Similarly, the 2015-2016 National Health and Nutrition Examination Survey (NHANES) data report obesity (BMI ≥ 30 kg/m^2) in 39.6% of the U.S. adult (≥20 y/o) population.[2] Therefore, weight loss remains an aspiration for people worldwide in an effort to improve health and reduce various co-morbid risk factors associated with obesity. Unfortunately, an exact cause or mechanism has yet to be pinpointed, and so many possible treatments are being explored.

Primary areas of treatment include diet, exercise, and medical interventions, each with their own varying degrees of success as well as pitfalls. Yet, long-term maintenance of weight loss is a consistent struggle across all areas. While dietary modification and increased levels of physical activity may remain steadfast recommendations, consumers, healthcare practitioners and medical professionals continually seek alternative strategies in the form of dietary supplements. As such, some ingredients are frequently used for weight loss such as fiber, appetite suppressors, lipolytic agents, and stimulants like caffeine and ephedra to name a couple.

Commonly, objections to the use of dietary supplements are that they often contain the aforementioned stimulants designed to increase metabolism. As such, consumers and

healthcare practitioners are wary of such formulae; hence, continued investigation of stimulant and non-stimulant supplements is warranted. For example, the use of a newer supplement Dichrostachys glomerata (DG), which shows potential antioxidant and hypoglycemic properties. Recent reports have stated occurrences of significant improvements in BMI, waist circumference, body fat, blood pressure, blood cholesterol, triglycerides and glucose, in obese (normoglycemic, type-2 diabetic, metabolic syndrome) patients. Also purported, was significant loss of weight (≈7-11 kg) and fat (≈3-5%), compared to placebo (≤1 [kg; %], respectively), over a two month period at 200-800 mg, 30-60 min before eating, 1-2 times per day.[3-5]

Other nutrients of interest are caffeine, capsaicin, and ashwagandha. Caffeine is a known stimulant and a defining constituent of coffee, tea, and energy drinks. It is also commonly used in dietary supplements targeting weight loss as a means of increasing thermogenesis, energy expenditure, and fat oxidation. Hence, it is thought to contribute to weight loss and maintenance, having some success.[6-9] Capsaicin shows to improve fat metabolism, appetite suppression and with caffeine suppresses hunger, increases feelings of satiety, and increases postprandial thermogenesis.[10-26] Ashwagandha improves weight and body-fat loss, muscle strength, stress, and mood. [27-35]

Thus, for this current study design, we examined two multi-ingredient nutritional supplement formulations using DG, whereby one contained caffeine (stimulant) and the other did not.

The aim of this study was to examine whether or not including DG to a weight loss supplement with or without caffeine ([WL+C] DG, clubmoss, caffeine, ashwaganda,

capsaicin; [WL] DG, ashwaganda, bioperine, capsaicin, rhodiola rosea, L-theanine, clubmoss, bacopa monneri) affects weight loss in the absence of an exercise or diet intervention vs. a placebo (6g dextrose). The study took place over 12 weeks, with a primary focus on change in body weight. A secondary aim included body composition, other indices of anthropometry, blood chemistries relating to hepatorenal function, and hunger and satiety. Tertiary aims were components of metabolic syndrome summed and presented as z-scores (MetS-z), physical activity, potential side effects, and sleep effects. We hypothesized that the nutritional supplement formulation examined would produce significant weight loss, whether containing caffeine or not.

Statement of the Problem

Will weight loss, body composition, and cardiovascular health be affected by prolonged supplementation of a novel weight loss formula, with and without stimulants, in the absence of a secondary intervention such as exercise?

Purpose

The purpose of this study was to investigate if ingesting a weight loss supplement containing dichrostachys glomerata, with and without caffeine, promotes weight loss in individuals maintaining their usual diets and exercise practices.

General Study Overview

Sixty-eight apparently healthy men and women (age 30-45) were recruited to participate in a double-blind, parallel group, stratified random, placebo-controlled trial examining the effects of two weight loss supplements (stimulant and non-stimulant) vs. a placebo control (6g dextrose). Supplements were ingested BID, with the stimulant formula containing 125 and 150 mg of caffeine for morning and afternoon doses, respectively. Participants were assessed at baseline and every 28-40 days (12-day buffer) for respective indices, over 12 weeks. Additional supplements were available pro re nata.

Study outcomes (dependent variables) included; body weight [*primary outcome*]; body composition (fat/fat-free mass and body fat percent), anthropometrics (BMI and waist-to-hip ratio), blood chemistry measures (clinical health markers: ALP, AST, ALT, creatinine, BUN, CK, LDH, glucose, cholesterol, HDL, LDL, TG, and CBC with platelet differential), hunger and satiety, resting energy expenditure, and diet characteristics [*secondary outcomes*]; physical activity, side and sleep effects [*tertiary outcomes*].

To examine the effects of the supplements on weight loss, control measures were utilized. As an entrance criterion, for homogeneity, participants needed to be moderately active (≤3-4 d/wk), with a BMI of 25-34.9 (Overweight to Class I Obese). If medications were required, for metabolic-related issues, they needed to be in use for six or more months. At baseline, measures were taken, and groups assigned; (A: WL+C) Weight loss formula + caffeine, (B: WL) Weight loss formula without caffeine, or (C: PLA) Placebo. Stratified random grouping was used to balance five parameters; BMI, body-fat percent (via dual-energy x-ray absorptiometry [DEXA]), average step count, sex, and age.

Hypotheses

$H_0$1: Body weight will decrease significantly in treatment groups compared to baseline and/or placebo

$H_0$2: Body composition will improve significantly in treatment groups compared to baseline and/or placebo

$H_0$3: Clinical health and safety markers will improve significantly in treatment groups compared to baseline and/or placebo

$H_0$4: Resting energy expenditure will improve significantly in treatment groups compared to baseline and/or placebo

$H_0$5: Diet characteristics in treatment groups will not significantly differ from baseline and/or placebo

$H_0$6: Reported hunger and satiety will significantly decrease and increase, respectively, in treatment groups compared to baseline and/or placebo

$H_0$7: Reported sleep quality in treatment groups will not significantly differ from baseline and/or placebo

$H_0$8: Reported side effects in treatment groups will not significantly differ from baseline and/or placebo

Delimitations

The study was conducted within the following parameters:

1. The study population was limited to overweight and sedentary men and women recruited from the College Station, TX area.
2. Participants were between ages 30-45; BMI 25-34.9 kg/m^2; and active ≤ 3-4 d/wk.
3. Participants' weight did not change ±10 lb within three months prior to screening.
4. Participants were not be pregnant or nursing within the past year, with no intent to be.
5. Participants did not have any uncontrolled metabolic disorders.
6. Participants were not currently, nor in the past 3 months, using dietary supplements for any condition or reason; otherwise, physician clearance was needed prior to start.
7. Participants were asked not to make lifestyle alterations for the duration of the study.
8. Those eligible attended a familiarization session to review study protocols; complete an informed consent and general health screening; as well, measure anthropometry.

Limitations

1. Recruitment was not truly random due to the limitation of Bryan/College Station, Tx, and those whom responded to recruitment fliers and emails.
2. Testing sessions were performed at similar times for the duration of the study.
3. Subjects may not have followed the supplement instructions as defined.
4. Dietary data collected was self-reported, via four-day food logs.
5. To reduce chances of error, equipment calibration abided manufacturer guidelines and samples were run in duplicate. Innate equipment limitations may have still persisted.

Assumptions

1. Health screening questions, for eligibility, were answered honestly and accurately.
2. Subjects followed the protocol explained to them during the familiarization session.
3. Prior to each testing session, participants fasted 10-12 hours; did not consume alcohol or use NSAIDS for 24 hours; and refrained from exercise for 48 hours.
4. Participants honestly and accurately completed the four-day food records.
5. Participants complied with their assigned supplement regimen.
6. The sample population was normally distributed.
7. The variance among the population sample was approximately equal.
8. All testing procedures was performed consistently, amongst lab personnel.
9. Laboratory equipment was functioning and calibrated prior to all testing sessions.
10. Subjects and researchers remained blinded to the supplements throughout the study.

CHAPTER II

LITERATURE REVIEW

An ever-growing problem in modern society is the apparent encroachment of obesity around the world. Due to its multifaceted nature, and involvement with physiological systems, we currently lack a full understanding of the mechanisms at play. Although the relationship between food quality, energy intake and expenditure is known and a matter of common knowledge, it does not appear to be the sole correlate. Thus, it is clear there cannot be any one single intervention rather; an amalgamation of many is likely necessary, prompting continued research into less studied and/or ancillary interventions. And so, the purpose of this literature review is to convey the incidence and etiology of obesity, highlight prevalent health complications thereof, outline and assess the effectiveness of key intervention techniques, and delve into supplement use as an intervention with a focus on those showing promise yet, require more research.

Obesity

Prevalence & Etiology

Obesity, a now recognized disease, has arguably reached the level of a pandemic according to the most recent data trends, which calculated approximately 266 million (10.8%) men and 375 million (14.9%) women (≥18 y/o) to be obese (BMI ≥ 30 kg/m^2), of them 58 million men (2.3% of all men) and 126 million woman (5% of all women) are classified as severely obese (BMI ≥ 35 kg/m^2), as of 2014. This same collaborative source suggested, in 2014, the global prevalence of obesity could reach 18% of men and surpass

21% of woman, with severe obesity making up 6% and 9% of those men and woman, respectively, by 2025.[36] Consonantly, the World Health Organization (WHO)[1], as of 2016, placed global prevalence of obesity (BMI ≥ 30 kg/m^2) and overweight (BMI ≥ 25 kg/m^2) adults (≥18 y/o) at 13% (650 million) and 39% (1.9 billion), respectively, with 11% obese, 39% overweight men and 15% obese, 40% overweight women. Nevertheless, obesity is certainly acknowledged on an epidemic level in many places, for example the most recent National Health and Nutrition Examination Survey (NHANES) data, from 2015-2016, reports obesity (BMI ≥ 30 kg/m^2) in 39.6% of the U.S. adult (≥20 y/o) population, 37.9% and 41.1% of men and women, respectively.[2]

When talking about the cause(s) of obesity it is almost impossible to pinpoint any one cause or reason, because it has come to be known as multi-factorial in origin, due to its roots in environmental influences, behavior and lifestyle, socioeconomic status, geographic location, physiology, and even genetics.[37,38] Despite this, there is a common anecdote used to describe the primary cause of obesity "energy in vs. energy out", stating that obesity stems from consuming more energy than is expended, thus leaving extra to be stored.[1] Fundamentally this holds some merit, as it follows the straightforward logic of the first law of thermodynamics. Although hypothetically, energy imbalance as the cause would be paradoxical, in that simply reversing it or balancing intake and output has not been working overall. The WHO[1] addresses reasons why this may occur, discussing increased intake of high-fat and energy-dense foods, convenient modes of travel and more sedentary jobs causing decreased physical activity, plus environmental factors related to

policies, food access and processing, and general education. Undoubtedly, all play a role in the etiology of obesity as a major health problem, as such requires consideration.

Health Complications

Obesity is associated with many poor health outcomes and comorbidities, the most well-known being the endocrine-related disorder Type 2 Diabetes Mellitus (T2DM). Other related health conditions include cardiovascular diseases (e.g. heart disease or stroke), musculoskeletal disorders (e.g. osteoarthritis), and even certain cancers (e.g. colon, renal, or ovarian) to name a few.[37,39] In fact, the criteria for what is now known as Metabolic Syndrome are a collection of key signs and symptoms put together to serve as a screening method to assess a patients potential risk for developing T2DM.[37,40] In general, clinicians look for distribution of fat around the visceral cavity (waist), hypertension (elevated blood pressure), low levels of high-density lipoprotein (HDL) cholesterol, increased levels of glucose, and high levels of triglycerides in the blood.[37] It is obvious to see that these criteria fit other complications as well; suggesting the parameters for Metabolic Syndrome may just serve as good warning signs as opposed to diagnostic criteria. Metabolic Syndrome and Obesity share many commonalities and are both linked to T2DM, wherein if Metabolic Syndrome were kept as a risk assessment tool, and not a separate diagnosis, it would further highlight the need for obesity/weight loss interventions.

Weight loss Interventions

Within the past few decades, more so than any time prior, there has been a consequent uptrend in possible weight loss and/or management interventions, the most prominent being lifestyle based. Conceivably, this is in response to rising rates of obesity,

but has seen mutable success typified by "human error", with compliance likely being a problematic factor. Lifestyle interventions such as behavioral, diet, and exercise remain the preferred method for both weight loss and maintenance, short and long term. In opposition of this, obesity rates continue to climb, leading to more alternative medical interventions inclusive of medications and surgery, attempting to combat obesity. The following sections will discuss these weight loss interventions.

Lifestyle

Behavior. Often weight loss programs operate under the assumption that changes regarding a person's behavior, diet, and physical activity are required, irrespective of any initial intervention used.[41-44] However, each component of "lifestyle interventions" are, to some degree, capable of acting alone. Behavioral modifications are often lumped in with diet and/or exercise, as they can be one in the same. Behavioral changes, in absence of secondary intervention, have shown average weight loss of ~3 kg (95% CI: 4.02-2.01) in 12-18 months by self-monitoring diet, exercise, weight[45,46] or reducing speed of intake[47], for example. In this context, behavioral change refers to identifying healthy food items, eating habits, altering daily routine and/or route of travel to avoid fast food establishments, eating in front of a television less, and other actions like this.

Dietary. This receives a lot of attention when it comes to weight loss interventions, with much emphasis on the concept of calorie intake compared to calorie output. Thus, caloric restriction of 500 kcal/d, a reduction by 30% daily kcal needs, or a limit of 1200-1500 and 1500-1800 kcal/d for women and men, respectively, with the goal of negative energy balance, are general dietary recommendations for weight loss.[37,48] As a result, there has

been back-and-forth about whether to restrict fat or carbohydrate intake; a 2014 meta-analysis of 7,286 people concluded that weight loss does not differ significantly (6 mo ≈ 8 kg/ea; 12 mo ≈ 7 kg/ea), either way.[49] The implication being, weight loss is achievable through caloric restriction of any nature, primarily short-term. An argument is therefore made to focus on improving diet quality, yielding similar results with normal calorie intake, but is significantly more effective in long-term maintenance and sustainable because it accounts for the weight- and calorie-independent effects (good or bad) dietary habits have on cardiovascular and metabolic disease risk.[39,50] A few examples of recommendations focused on building positive eating habits with quality intake are the DASH, Mediterranean, and Heart Healthy diets, the details are provided in *Table 1*.

Table 1: Overview of Key Clinical Diets

Diet	CHO/Fat/Pro (%)	Emphasis	Limit	Rationale
DASH: [51-53]	55/27/18	Vegetables, fruits, low-fat dairy products, whole grains, poultry, fish, beans, and nuts potassium, calcium, magnesium, and fiber	Sweets, sugar-sweetened beverages, red meat, saturated fats, sodium (2,300 mg/d)	Lowers BP, lipids, and CVD risk
DASH-Sodium: [52,54]	55/27/18	Same as DASH	Same as DASH; Sodium (1,500 mg/d) (U.S. avg 3,600 mg/d)	Lowers BP more than DASH
DASH+: [51,54]	48/27/25	DASH; Increased protein	Same as DASH	Lowers BP and lipids more than DASH
	48/37/15	DASH; Increased unsaturated fats	Same as DASH	
Mediterranean: [53,54]	55/30/15	Plant-based foods, fruits, vegetables, whole grains, legumes, nuts, olive oil, fish and poultry (≥2x's/wk), eggs (≤4x's/wk)	Red meat (monthly), saturated fats, wine, sodium	Lowers BP, glucose, lipids, and CVD risk
PREDIMED: [55-57]	43/37/15	Mediterranean; Increased unsaturated fats (extra virgin olive oil or nuts)	Same as Mediterranean	Lowers BP, glucose, and lipids more than Mediterranean
RESMENA: [58,59]	40/30/30	Mediterranean; 7 meals/d, polyunsaturated fatty acids (n-3 PUFAs), antioxidants, low glycemic carbohydrates	Same as Mediterranean; High glycemic carbohydrates	Lowers BP, oxidative stress markers, triglycerides; increased LDL cholesterol
Heart Healthy: (AHA) [58,60]	55/30/15	Fruits, vegetables, whole grains, fish, legumes, and poultry	Trans fats, added sugars, red meat, sodium, and saturated fats	Lowers BP, lipid profile, and CVD risk

DASH; Dietary Approaches to Stop Hypertension, PREDIMED; Prevención con Dieta Mediterránea, RESMENA; Reducción Del Síndrome Metabólico Navarra-España , AHA; American Heart Association, CVD; Cardiovascular Disease, BP; Blood Pressure

Exercise. Physical activity is the final, and arguably most established, of the lifestyle interventions. The current recommendations for adults, in the U.S., suggest aerobic physical activity (e.g. running, power-walking, etc.) at either a moderate-intensity for 150-300 min/wk, a vigorous-intensity for 75-150 min/wk, or a combination of both and muscle-strengthening activities ≥2 d/wk.[61] Following these guidelines, health benefits have been reported independent of weight loss, as early as after a single bout. Such improvements include blood pressure, insulin sensitivity, sleep, anxiety, and "day-of" cognition, most showing greater improvement with increased regular activity. Reduced disease risk (i.e. cardiovascular/metabolic) appears as a function of time and consistency in following an exercise program.[62]

Exercise has been studied for far longer than the previously discussed interventions and is still, anecdotally, believed by many to be the most and maybe the only important factor when it comes to weight loss and maintenance. Obviously, this is an oversimplification but, it does accurately highlight the impact physical activity can have and simultaneously ignoring the consequences of a one-sided weight loss program. For example, resistance training without dietary adjustments may increase lean mass with little to know effect on fat mass or cardiovascular health, sometimes having a negative influence[63]; similarly, aerobic training without dietary adjustments might reduce fat mass as well as lean mass, in extreme cases result in severe health complications.[63] Meta-analysis of trials indicate dietary changes alone, over a 12 month period, can lead to weight loss of ~1.38 kg, while the addition of regular exercise resulted in a loss of ~3.34 kg, retaining a greater weight loss for up to 2+ years.[64] Interestingly, the type of physical

activity (aerobic or resistance; high or low intensity) do not appear to be effectively different in overall weight loss, with the concession that a higher intensity tends to lose weight quicker.[65] Congruently, if the interventions are paired in the wrong way, i.e. intense and frequent exercise with calorie restriction, the initial result is drastic weight loss typically followed by weight regain (sometimes more than lost) and a decreased and altered resting metabolism that seemingly favors fat storage lasting 6 years or more.[66]

Related, is the often-overlooked behavioral aspect. Physical activity (and diet) can be effective, especially short-term, but, for long-term maintenance and avoiding potential complications, the interventions need to be realistic and sustainable for the individual. According to the Physical Activity Guidelines for Americans, only 26% of men and 19% of women report meeting activity (aerobic and resistance) guidelines.[61] In the look AHEAD trial, ~68% of participants lost ≥5% of their initial body weight at year 1 (avg loss ~8.5%) compared to ~50% (25.8% had lost 5-10%) of participants at year 8 (avg loss ~4.7%); wherein activity levels doubled at year 1, decreasing by year 4 (avg loss ~4.4%), and dropping almost back to baseline levels by year 8.[67]

Medical

While lifestyle interventions are a steadfast, making great strides and work for many people, they are not without their faults. A usual intervention expects to see and sustain between 5-10% weight loss, within 6 months, often failing in this goal.[60,68] Regardless of the efforts made, the obesity rate continues to climb worldwide. Several global agencies release guidelines addressing these and other facets, updating them periodically based on current research.[43,44,69,70] Due to the ongoing nature of treating

obesity, many medications, surgical procedures, and devices were created as additional/ supplementary to lifestyle interventions and is the focus of this section.

Medication. As far as medication is concerned there are many known to have effects on weight, some intended and some not. More often, classes of drugs will have similar influences on weight. For instance, antipsychotics, antihistamines, adrenal steroids, and adrenergic blockers either have no effect or lead to weight gain, the latter medication being largely neutral. In comparison, medications such as antiepileptic/anticonvulsants, antidiabetics, and mood stabilizers/antidepressants have an equal chance of going in either direction, the latter favoring weight-gain.[71] On the other hand, there are medications intended for the treatment of obesity. These medications are typically long-term (e.g. pancreatic enzyme inhibitors) and have shown weight loss anywhere from 3-15% body weight within 1 year, whereas the lesser used short-term medications (<12 wks; e.g. Trace-amine associated receptor-1 [TAAR1] agonists) lead to an average loss of 5-10% body weight over 12-28 weeks.[37,72-74] The regulatory guidelines on use of pharmacotherapy to treat obesity states that individuals (BMI $\geq$ 27 kg/m^2 with comorbidity; or $\geq$ 30 kg/m^2) who fail to achieve and/or maintain clinically meaningful weight loss ($\geq$5% body weight) are eligible for medication to assist a management program; however, behavioral, diet, and exercise (lifestyle) modifications are promoted in obesity management for BMI $\geq$ 25 kg/m^2.[50,75] Any medication is deemed ineffective and recommended to cease if the patient losses < 5% of their body weight after 3 months.[75] See *Table 2*.

Surgery/Devices. Surgical procedures and medical devices are akin to medications in the sense that their intended use is for when lifestyle interventions do not appear effective by

themselves. In that scenario the Endocrine Society recommends that bariatric surgery be considered if the patient also has a BMI ≥ 35 kg/m^2 with comorbidity or ≥ 40 kg/m^2.[75] Bariatric surgeries include; sleeve gastrectomy, involving the placement of staples along the curve of the stomach from esophagus to small intestine, narrowing the stomach, followed by excision of the other half (1.3% re-operation; 5.5% complications); and gastric bypass, the most common being Roux-en-Y, which is the anastomosis of proximal stomach and small intestine that physically re-directs the path of foodstuffs through the gastrointestinal tract (1.8% re-operation; 10.7% complications).[76] Other variations of the gastric bypass procedure differ in where the anastomosis occurs, i.e. what sections of the small intestine and stomach are attached to one-another. Bariatric surgery seemingly "avoids" the metabolic backlash reported with rapid weight loss in intense diet and exercise programs.[66] Both cause metabolic rate to diminish, however, bariatric patients return close to pre-operation rates in 6-24 months[77], whereas lifestyle alteration shows diminished metabolic rates for several years after.[66,78] In relation, resting metabolic rate strongly correlates with fat-free mass (FFM) pre- and post-operation.[79] Here, better understanding of mechanisms are needed, as an argument can be made for the initial post-surgery drop being due to removal of a sizeable mass of metabolically active tissue followed by slow healing and adapting (returning to equilibrium) plus an inherent food quantity restriction. In contrast, FFM lost in intense exercise and diet is slower and from stimuli rather than removal.

Various devices also exist for managing weight, many of them requiring minimally invasive surgery. A well-known example is the gastric band, a fluid-filled band placed

under and around the gastro-esophageal sphincter where the constant pressure stimulates vagal afferent nerves, affecting the down-stream signaling of fullness. This procedure shows a ~7% re-operation and ~7.8% complication rate.[50] Other devices currently in use include; gastric balloons; electric stimulators systems (3.7% AE[80]); bypass liners; and an oral apparatus. *Table 2* provides a general list of other devices, surgeries, and medications with a brief description, the average weight lost and over what interval of time. One other device of interest is the gastric emptying system, e.g. Aspire Assist (*Aspire Bariatrics, King of Prussia, PA, USA*), which is a small aspirating system that removes up to 33% of a person's stomach content shortly after consumption, through a gastric tube in the abdomen, essentially mimicking bulimia nervosa with a machine. Of note, while this device has shown ~12-14% loss of body weight, it was paired with extensive lifestyle (behavioral) counseling, psychological evaluations and was compared to the ~4-5% loss seen in lifestyle counseling alone.[68,81,82]

Table 2: Medical Interventions

Treatment		Description	Weight loss	Interval
Medication:		*Controls/Limits Intake (chemically)*		
	Long-term	Pancreatic enzyme inhibitors, 5-HT and GLP-1 receptor agonists	~3-15%	1 yr [37,72,73]
	Short-term	TAAR1 agonists (releases monoamines)	~5-10%	12-28 wk [73,74]
Bariatric Surgery:		*Re-Directs/Limits Intake (functionality)*		
	Sleeve Gastrectomy	Staple placement along curvature of the stomach with removal of the closed-off half	~16.8-19.8%	6-18 mo [82]
	Roux-en-Y Gastric Bypass	Anastomosis of proximal stomach and small intestine at various points	~24.8% ~30-35%	6 mo [83] 1-3 yr [83,84]
Devices:		*Controls/Limits Intake (mechanically)*		
	Gastric Band	Fluid-filled band under gastro-esophageal sphincter, stimulating vagal afferent nerves	~10.3-18%	3 mo-20 yr [68,84,85]
	Intragastric Balloon	Swallowable pill which is filled, typically with fluid, and rests in the stomach	~6.6-12.2%	6 mo [86-89]
	Electric Stimulator	Electrodes in vagal nerve trunk, connect to neuro-regulator, influencing nerve signals: Vagal Block or Pacemaker	~9.2% ~13.3-15.7%	¦ 1 yr[90] 1-2 yr[91,92]
	Gastric Emptying System	Aspirating unit removes stomach content via gastronomy tube and port in abdomen	~12.1-14.2%	1 yr [68,81,82]
	Bypass Liner	Fluoropolymer sleeve, of various lengths, used to cover segments of the small intestine	~5-13.3%	6-12 mo[68,82,93]
	Oral apparatus	A mouthpiece occupies space, forcing smaller bites and slower intake	~7.3-11%	3 mo -3 yr[94]

¦; vagal block, GLP-1; Glucagon-Like Peptide, 5-HT; Serotonin

Supplements

As the previous sections indicate, lifestyle and medical interventions are still largely being studied relative to weight loss. However, an area in weight loss coinciding with diet is supplementation, excluding nutritional supplements for preventing/treating electrolyte imbalances or related conditions resulting from significant decrements of weight. Considering the overall success and limitations of dieting, discussed above, it stands to reason the next step would be to fine tune and/or simply add to a diet program, by way of supplements, attempting to improve weight loss outcomes.

Many supplements have garnered attention in this respect, such as thermogenic compounds including caffeine, ephedrine, or even capsaicinoids (commonly used as cayenne powder), to name a few. These are sought primarily for their purported ability to suppress appetite and/or increase satiety and the "thermic effect of food" (thermogenesis), evidently increasing resting metabolic rate and ultimately weight loss.[16,17,95,96] Whereas, supplements such as ashwaganda, bacopa monniera, clubmoss, rhodiola rosea, and theanine are investigated for their potential to reduce stress/anxiety, depression, and improve sleep, essentially affecting mood and vigilance, touching on the mental health influence in weight and health. Others including clubmoss, dichrostachys glomerata, and piperine are considered for their possible antioxidant, anti-inflammatory, or GI and bioavailability effects, where they have typically been incorporated with the purpose of accompanying or aiding other supplements to increase their effects.

However, many of these supplements lack a sizeable body of literature. Therefore, in an effort to understand the effects, possible mechanisms, and how it all might fit

together, these sections will review several of the aforementioned herbal and non-stimulant supplements believed to influence weight, as primary nutrients, as well as nutrients which work synergistically towards the same goal, such as caffeine.

Purported Primary Nutrients

Dichrostachys glomerata. DG is a spice used in Cameroon, said to have potential antioxidant and hypoglycemic properties. Recent reports have also shown DG to significantly improve BMI, waist circumference, body fat, blood pressure, blood cholesterol, triglycerides and glucose in obese, normoglycemic and type-2 diabetic, subjects when administered 400 mg (BID), 30-60 minutes before eating lunch and dinner (800 mg total). Participants exhibited weight loss of ~7.5 kg, with a little more than 3% drop in body fat, compared to placebo (-1.3 kg, -0.7%, respectively).[4] An essentially identical study, from the same group, also corroborated the antioxidant effects in obese, normocglycemic, diabetics (T2DM).[5] Similar responses to the former and latter experiments, again from the same group, were also observed in obese individuals with metabolic syndrome when administered 200 mg. This time participants dropped around 11 kg body weight, with an almost 5% decrease in body fat, compared to placebo (-0.5 kg, -0.2%, respectively).[3] However, this particular study's conclusions should not be taken at face value; due to the fact the amount given is never clarified. It is only ever apparent that participants received at least 200 mg per day, since the abstract states administration of "200 mg, 30-60 minutes before lunch and dinner", then contradicts this in their methods by stating "200 mg, 30-60 minutes before lunch or dinner", with no specified daily total.

Otherwise, DG shows some promise within the realm of weight loss and related complications but requires more research outside of this group.

Ashwagandha. Also known as Withania somnifera, this is an herbal adaptogen (substances which help attenuate damaging effects of stress) commonly used, in the Indian medical practice of Ayurveda, for a variety of health related reasons ranging from stress and cognition, to Alzheimer's disease and cancer.[27] It is more commonly known for its' potential anxiety reducing (anxiolytic) properties. Animal models, primarily mice and/or rats, have reported attenuating chronic and acute stress-related outcomes inclusive of glucose intolerance, increased stress hormones, gastric ulcers, male sexual dysfunction, and immunosuppression.[97,98] Ashwagandha has also been shown to have an additive benefit in rats given Diazepam, a common antidepressant, where the drug effects seemed to be enhanced.[99] Several related animal studies support the herbs prospects for neuroprotection[98], hypocholesterolemic[100], antioxidant[100,101], and anti-inflammatory effects.[102,103]

In human trials, evidence supports an anxiolytic effect while supplementing 125, 250, 500[28], up to 2,250 mg[29,32,33], reaching as high as 5g[30] and 12g[31]. Interestingly, some studies showcased other potential benefits such as cognitive improvements[34], weight loss[32], reduced body fat, improved muscle strength (w/o exercise)[35], stress relief, and antidepressant effects.[28-33] Ashwaganda has also been used to reduce chemo-therapy induced fatigue.[104] Yet, despite the seemingly promising research, there remains no real consensus on an effective dose or mechanism of action in either animal or human models. *Table 3* offers a list of mostly human studies, primary reported outcomes, and dose used.

Table 3: Primary and Synergistic Supplements

Supplement		Dose	Duration	Primary Outcomes	Notes
Purported Primary Nutrients					
Dichrostachys glomerata		200-400 mg	8 wk	Weight loss [3] ⌜Weight - DG: -11.15±0.18 kg | PLA: -0.53±0.11kg⌝ ⌞Fat - DG: -4.73±0.11% | PLA: -0.20±0.10% ⌟	
		800 mg	8 wk	Weight loss [4]* Antioxidant [5] ⌜Weight - DG: -7.67±0.36 kg | PLA: -1.32±0.21kg⌝ ⌞Fat - DG: -3.20±0.20% | PLA: -0.70±0.11% ⌟	* Normoglycemic, obese subjects. Obese T2-diabetics had similar results [4]
Ashwaganda (Withania Somnifera)		125 mg -12g	2-12 wk	Anxiolytic/Antistressor/Antidepressant; Weight loss; ↑ Cognition [28-34]	Stress focused [30]
		750; 1000; 1250 mg	4 wk	↓ Body fat; ↑Muscle strength (w/o Ex) [35]	
	(Rat)	0.75-1.5g	≤1-28 d	Antioxidant/Anti-inflammatory [100,103]	1 g/kg [103]; 0.75 & 1.5 g/d [100]
Capsaicinoid		2 mg	--	Minimum effective dose [10,11]	Meta-Analysis [10]; Review [11]
		≡ 3.09 mg	24-36 hr	↔ Satiety; ↓ Ghrelin; ↑ Metabolic Rate [12-14]	🌶 | ≈ 0.3% capsaicinoids
		≡ 4.59 mg	1-6 wk	↓ Appetite/↑ Satiety [13,15]	🌶 | ≈ 0.3% capsaicinoids
		≡ 30 mg	≤1-7 d	↑ Metabolic Rate; Lipid Oxidation; Thermogenesis [13,16,17]	🌶 | ≈ 0.3% capsaicinoids
	Capsinoids	6.9 mg	6 wk	↓ Appetite/↑ Satiety [15]	
	Capsaicin	≡ 0.19 mg	≤1-7 d	No effect [13,18]	🌶 | ≈ 0.3% capsaicin
		≡ 2.77 mg	≤1 d	↓ Appetite/↑ Satiety [18]	🌶 | ≈ 0.3% capsaicin
		≡ 1.2-6.75 mg	1 wk	Tolerable Dose; No other effects [13]	Ⓒ | ≈ 1.2-1.35% capsaicin
		≡ 6.75; 7.68 mg	36-48 hr	↓ Appetite/↑ Satiety [19,20]; ↑ Lipid Oxidation [21]	🌶 | ≈ 0.25% capsaicin
		≡ 18; 30 mg	≤1 d	↓ Appetite/↑ Satiety; ↓ Blood Glucose [22,23]	🌶 | ≈ 3 g/kg capsaicin
		26.6 mg	≤1 d	↓ Blood Glucose (maintained Insulin) [22,23]	🌶 | (5g) = 26.6 mg capsaicin
		135; 150 mg	≤1-84 d	↑ Lipid Oxidation [24,25]	
Purported Synergistic Nutrients					
Caffeine+	/[*Theanine*]	40/[9] mg	≤1 d	↑ Attention, Alertness; ↓ Tiredness [105]	
		40/[97] mg	≤1 d	↑ Attention [106]	
		50/[100] mg	≤1 d	↑ Vigilance, Attention, Memory [107]	
		150/[250] mg	≤1 d	↔ ↑ Vigilance, Memory; ↓ Tiredness, Headache frequency [108,109]	
	/[Capsaicin]	25/[0.2] mg	≤1 d	↑ Thermogenesis; No cardiac effects [26]	
		≡ 231/[4.59] mg	6 wk	↓ Hunger/↑ Satiety [15]	🌶 | (1530mg) ≈ 0.3% capsaicinoids
Piperine	(Rat/Mice)	0.5-20 mg/kg	≤1 d	↓ GI motility [110-113]	Review [112]
	(Rat/Mice)	20-142 mg/kg	≤1-56 d	↑ Gastric Acid Secretion; Bioavailabilty in humans (20mg/kg) [112,114,115]	
	(Rat/Mice)	1; 1.3; 4; 8; 16; 32 mg/kg	1-8 wk	↓ GI motility; Anti-diarrheal [110-113]	
L-Theanine		50 mg	--	Relaxant [116]	Review [116]
		100; 200; 250 mg	≤1 d	↑ Attention/Vigilance [108,117]; Antistressor; Anxiolytic/Relaxant [109,116-119]	
		400 mg	6 wk	Anxiolytic/Relaxant [120]; ↑ Sleep [121]	Review [116]
Rhodiola rosea		60mg	5 wk	Anti-inflammatory [122]	
		100; 144; 170; 400; 576 mg	1-4 wk	↓ Fatigue/↑ Cognition; Antistressor [123-127]	(144; 170mg) ≈ 2.3% Salidroside
		370; 555 mg	≤1 d	↓ Fatigue/↑ Cognition [128]	
		364 mg	6 wk	↑ Fatigue [129]	
		340; 680; 1020; 1360 mg	6-12 wk	Antidepressant [130-132]	
Bacopa monniera		225 mg	6 mo	↓ ADHD symptoms [133]	
		250; 300 mg	≤1d-12wk	↑ Memory/Cognition; Attention; Anxiolytic/Antidepressant [134-140]	
		300; 450 mg	12 wk	↑ Information Retention [141]; ↔ Attention, Cognition or Anxiety [141,142]	
Clubmoss		500 mg/kg	≤1 d	Anti-inflammatory [143]	
	Huperzine-A	0.03-0.45 mg	--	↑ Memory/Cognition [144]	Review [144]
	(Cell culture)	100 nM	--		

🌶: Reported as Capsicum/Red Pepper/Cayenne; Ⓒ: Capsimax; ≡: Calculated, Refer to Notes; ↔: No Change; ↑: Increase; ↓ Decrease

Capsaicinoids. The compounds found in chili-peppers (Capsicum genus) responsible for the "hot" sensation felt when eaten, or contact is made with a mucus membrane (e.g. eyes or nostrils). This is due to their binding of the nociceptor group associated with transmitting signals of burning or acidic pain.[11,145] There are many molecules classified as a capsaicinoid, all of which are relatively similar in structure, with capsaicin and dihydrocapsaicin approximating 90% of the total structures on average.[146] That being said, capsaicin is considered to be the primary active constituent, causing the previously mentioned side effects, along with likely being responsible for any medicinal properties.[145]

In the same way, there are various naturally occurring capsinoids that happen to be structurally akin to capsaicin, subsequently exhibiting similar effects related to appetite suppression, with the primary difference being the lack of a burning sensation.[15]

Capsaicinoids, mostly capsaicin, are reported to have roles in pain relief [147], weight loss/management[10,11], thermogenesis[17], anticancer therapy and antioxidant activity.[146,148] Supplementation in humans has concluded that 2 mg of capsaicinoids is the minimal effective dose, even causing some appetite suppression.[10,11] However, the amount of capsaicin involved is not clear for this recommendation. The studies reporting on capsaicinoids as a whole have shown increases in metabolic rates, appetite suppression, satiety, lipid oxidation, and thermogenesis using 3.09, 4.59, and 30 mg of capsaicinoids, which are doses calculated from the total dose of the supplement given (e.g. cayenne powder) and reported as 0.3% of total dose.[12-17] Fortunately, capsaicin data exists reporting average doses of ~2 mg, with 0.19 and 1.2-1.35 mg (reported as 0.3% and 1.2-1.35% of total supplement dose, respectively) having no effect, while 2.4-2.7 and 2.77 mg (reported as 1.2-1.35% and 0.3% of total supplement dose, respectively) show tolerability, appetite suppression, and increased satiety.[13,18] Other studies have tested capsaicin doses ranging from 6.75 to 150 mg, having an almost consistent outcome of appetite suppression and increased satiety[19-21,23], with increased lipid oxidation and glucose uptake maintenance being less frequent but, prevalent.[21-25]

The sensation of burning pain, mentioned earlier is recognized by the Transient Receptor Potential Vanilloid subtype-1 (TRPV1) receptor family, which typically activate at temperatures ≥40°C (104°F) or in acidic conditions like a drop in pH from 7.4 to 6.3

(Noxious stimuli) via binding of vanilloid compounds, therefore allowing the sensation of warmth or burning.[149,150] For example, if a room was too hot the TRPV1 receptors would eventually be activated, ultimately stimulating a cascade geared toward assessing the heat for danger and/or worsening pain, and to some degree, stimulating the central nervous system to activate thermoregulatory processeses.[150] Capsaicin has a vanilloid-like structure and is therefore able to bind TRPV1 receptors, activating the sensory signal cascade responsible for feeling its trademark burning pain, hence why these receptors are also known as "capsaicin receptors". Subsequently, it could stand to reason that capsaicin might cause reactions such as sweating, among other things, as a thermoregulatory response.[151] In this regard, there is a potential explanation for hunger suppression, given capsaicin's analgesic-like effect through desensitization.[149] However, more research needs to be done in relation to mechanisms.

While data does support many of the claims, much of the human data are not consistent and lack clear mechanisms of action. This may be due, in part, to inconsistent supplements as well as reporting, where using cayenne and red chili's/capsicum is concerned. Many studies will convey "capsaicin" was administered at the milligram dose actually used for the supplement the capsaicin was in (e.g. cayenne or chili); or they will describe the amount and/or percent capsacinoid content but, will go on to report only about capsaicin without assigning and value to it, making consistent dose effects difficult to assess. See *Table 3* for examples.

Purported Synergistic Nutrients

Caffeine. A well-known component of coffee, tea, and energy drinks, estimates suggest that ~85% of adults living in the U.S. regularly consume caffeine in some form.[152] Caffeine is a methylxanthine that stimulates, broadly, the central nervous system, muscle, and heart. It also increases gastric activity such as acid secretion, motility, and acts as a diuretic.[153] It has been shown to increase thermogenesis, dose-dependently[7], energy expenditure, and fat oxidation.[9] Hence, it has been connected to weight loss, with some success in loss and maintenance[8]; possibly contributing via increased fat oxidation from sympathetic activation of the CNS along with increasing fluid loss.[6,7] Habitual use however, may lead to caffeine tolerance and diminished effects.[6] Caffeine has the ability to interact with the body and metabolism in far too many ways for the scope of this review so, here (*Table 3*) some prominent roles caffeine may play in weight loss and in combination with other supplements are highlighted.

Presently, there are not many experiments showing caffeine in combination with the supplements discussed above, aside from theanine, capsaicin, and mixtures of multiple ingredients, indicating a need for this research given the popularity of some combinations in commercially available products. Caffeine (25-231 mg) reported in combination with capsaicinoids/capsaicin (0.2-4.59 mg) shows to increase thermogenesis and satiety, plus, reduce hunger.[15,26] For healthy adults, caffeine intake up to 400-500 mg/d poses no real safety concerns[154,155], correspondingly, 3-6 mg/kg is recommended for ergogenic effects in trained populations.[156] Then again, sleep disturbances, nervousness, jitters and shaking,

with possible toxicity, may occur with intake of 15 mg/kg, leading to nausea, vomiting, tachycardia, seizures, and cerebral edema.[153]

Piperine. Piperine is the active component of Black Pepper, a well-known food ingredient and spice, having been attributed various benefits related to health and well-being. In Ayurveda Black Pepper is believed to mostly benefit oxidative damage, inflammation, hypertension, and fertility.[157] One well established action, in animal and human trials, is its ability to increase bioavailability of compounds paired with it, curcumin being one of the more studied of them.[114] Deriving from that research, using 20 mg/kg, is the suggested dose of 20 mg to aid in the bioavailability of a substance. The other influence it is most known for having is increasing gastric secretions, slowing the rate of gastric emptying, and intestinal transit times in mice/rats[110-112], likely contributing to bioavailability of a substance, although not corroborated in humans. Piperine has also been shown to stimulate CNS activity and, in conjunction with capsaicin, shows promise as an analgesic through binding of the Vanilloid receptors found in both the central and peripheral nervous system.[147,157] An important distinction is, the vast majority of documented effects observed and tested are in animal models and, while relevant and necessary, human data is currently limited (see *Table 3*).

Theanine. L-Theanine is an amino acid, non-proteinaceous, with a similar structure to glutamine. It is purported to have benefits in several related areas of mental processes, given its ability to cross the blood brain barrier and directly affect metabolism in the brain.[158,159] Thus, given its structural similarity and ability to enter the brain it is not surprising that animal models have shown theanine interact with various aspects of

glutamate metabolism and γ-aminobutyric acid (GABA).[118] Human trials (*Table 3*) reported exhibiting more "sedative" outcomes, such as; decreased stress, improved sleep, relaxing, and anxiolytic effects at 50, 200, 250, and 400 mg.[109,116-121] In direct contrast to this, increases in attention and aspects of vigilance were demonstrated at 100 and 200 mg.[108,117] A 2016 systematic review attempted to reconcile some of these data, focused on studies using 200-400 mg of theanine, and concluded supplementation could help reduce acute stress and anxiety but, only to individuals experiencing the acute stressors at the time of ingestion, i.e. not likely to help with generalized or chronic problems.[160] There has also been research showing the effects of caffeine partnered with theanine and capsaicin, separately. Caffeine with theanine has shown improvements in attention, vigilance, memory, and decreases in reported tiredness or exhaustion following administrations of 40-150 mg caffeine paired with 9-250 mg theanine.[105-109]

Rhodiola rosea. Another adaptogenic herb, also used in Eastern medicine for heart disease as well as depression[161] and anxiety[131], rhodiola rosea has also been associated with a litany of other benefits for instance, decreased fatigue[125], cognitive dysfunction[162], antioxidant[163], neuroprotective[164,165], and anti-inflammatory effects.[122] Although most of the results come from animal and cell culture models, there are a fair number of human studies which show anti-inflammatory[122] and antidepressant[130-132] effects, plus reductions in fatigue and stress[123,128] with improvements in cognitive abilities[126,127] using dosages of 60 up to 1360 mg, *Table 3* lists dosage details. In opposition, several systematic reviews and meta-analysis' as recently as 2016 have gone over the available human data and concluded that not only is there not enough but, a lot of what exists is not reliable. For

several previously mentioned outcomes this conclusion was unanimous in four different reviews, spanning four years (2011, -12, -14, and -16), each with a different focus; e.g. trial design[166], fatigue (physical and mental)[167], heart disease[168], and cognition with emphasis on Alzheimer's disease[169]. All acknowledged the potential this herb has, based on animal and cell models, they also agree existing human research was not properly controlled or tested in most cases and often over extrapolated.

Bacopa monnieri. Bacopa monnieri is another herbal adaptogen used in Ayurvedic medicine, primarily associated with affecting memory and cognition. Other health claims are related to improved attention, anxiety and depression as well as antioxidant, anti-inflammatory, and antidiabetic effects.[170] Evidence supports the use for aiding stress and anxiety relief[171], in mice, and also for anti-depressant capabilities.[171-174] Collectively, this interaction is purported in relation to the dopamine and serotonin systems. Diabetic rat models have observed anti-hyperglycemic[175] (preventing high serum glucose) as well as anti-hyperlipidemic[176] activity, suggesting a role in treating diabetes. Other research, in mice and rats, indicates potential anti-inflammatory[177], antioxidant, and neuro-protective functionality too.[178,179]

Unfortunately, studies performed with humans are less clear; having yielded mixed results (see *Table 3*). Currently human research with bacopa monnieri has the most support for improving memory and cognitive abilities, predominantly exhibited with a 300 mg dose[135-140] but, has also been shown using 250 mg.[134] Investigations using 300 mg have also proposed anxiolytic and antidepressant properties[136,137,140], even improvements in overall attentiveness.[136] A 2014 study sought to examine attention-deficit hyperactivity

disorder (ADHD) symptoms in an adolescent population, resulting in an overall reduction in such symptoms as impulsivity, restlessness, and attention with 225 mg.[133] Despite some evidence with different amounts, 300 mg is most commonly tested and so it possesses the larger number of associated benefits. As such, it has taken on the role of "suggested dose" without regard for the lack of scientific literature establishing a recommendation. Conversely, bacopa monnieri has demonstrated no effect on attention, cognition, or anxiety at 300 or 450 mg but, still had improvements in new information retention.[141,142] Thus, the verdict is not out yet on memory and/or cognitive effects.

Clubmoss. Also known as Devil's Claw, is used in Eastern medicine for its effects on memory, wound healing, and as an analgesic.[143] Generally, the healing claims have been demonstrated in mice at 500mg/kg (clubmoss), resulting in anti-inflammatory effects in response to experimentally induced damages.[143] Other research, looking at memory, focuses on the main active component, Huperzine-A, due to the neuroprotective properties exhibited in human cell cultures as a cholinesterase inhibitor.[180] Mouse models have reported enhanced learning and memory, showing cholinesterase inhibition, suggesting Huperzine as a potential treatment for Alzheimer's disease.[181] The primary obstacle in the literature is the weak presence of human trials, wherein existing dose recommendations stem from a 2006 review stating 0.03-0.45 mg improved subjects' memory and cognition. Conversely, a more recent (2013) meta-analysis concluded Huperzine-A (0.02-0.8 mg) seemingly yields some memory and cognitive benefits but, a wider dose margin was assessed than the 2006 review, additional studies are required with better, more clear methodologies/reporting. As a result, directives were given to take the results with care.[182]

Summary

Taken all together, obesity is a growing problem worldwide that has been assessed by many different disciplines with mediocre success, at best, when weighed against the grander scheme of things. Major strides have been made towards treating this condition within medicine, dietetics, and exercise physiology showing great success both individually and concomitantly. Despite this, collectively we are far from overcoming the obstacle that is obesity, suggesting a need for more research and possibly further extension into other areas of study. One such region to consider is supplementation, herbal or otherwise. Ample research has come forward in recent years about some supplements including Ashwaganda, Bacopa monniera, Capsaicinoids, Clubmoss, Dichrostachys glomerata, Piperine, Rhodiola rosea, and Theanine where some were paired with another or even with caffeine, with promising results, *Table 3* summarizes research, primarily human, for each of these nutrients. Exploration into this realm is still in its infancy and requires more support, specifically with regards to human trial data looking at individual and combined supplementation, in order to more definitively tease out individual or synergistic mechanisms and benefits.

CHAPTER III

METHODS

The purpose of the present study design was to assess prolonged supplementation responses for two novel weight loss formulas, one containing a stimulant (WL+C) and the other not (WL), in the absence of a secondary intervention such as exercise. Supplements or placebo were ingested for a 12-week period and assigned in a double-blind, parallel, stratified random manner, with repeated measures. The study was performed in the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University, with approval from Texas A&M University Institutional Review Board (IRB2016-0829FX) and signed informed consent from each participant. The ensuing sections review the procedures used and thereafter, detailed methodologies.

Participants

Sixty-eight apparently healthy, recreationally active men (N=31) and women (N=37), between ages 30 and 45 (avg 37±5 yrs), were recruited to participate in this study. Individuals who expressed interest via response to study email or flyer advertisements were asked to come in for an interview, to determine if they met initial screening eligibility for participation in this study. Those who met initial screening qualifications then attended a familiarization session where the details of the study were explained, human subject consent forms were signed, personal and medical history information was collected, and the participant had a general clinical physical exam, to determine further eligibility.

Participant Inclusion Criteria

Eligibility required subjects be healthy, moderately active (≤3-4 d/wk), men and women ranging 30-45 years of age with a Body Mass Index (BMI) between 25 and 34.9 (Overweight to Class I Obese). Participants taking medications for hyperlipidemia, hypertension, glucose regulation and thyroid conditions were eligible if the medication had been taken for a minimum of six months prior to starting the study.

Participant Exclusion Criteria

Participants were ineligible if they; had a recent history of weight change (±10 lb) within three months prior to their start date; had uncontrolled metabolic or cardiovascular disorders, heart disease, hypertension, arrhythmias, diabetes, hypogonadism, hepatorenal, musculoskeletal, autoimmune, neurologic or thyroid disease, or known electrolyte abnormalities; drank excessively (≥12/wk); were currently taking medications (except birth control) for less than six months; consumed dietary supplements for thyroid, hyperlipidemia, hypoglycemia or weight loss (e.g., ephedra or thermogenic compounds, etc.) three months before the start of the study; currently, recently (within the past year) or were planning to become pregnant and/or lactating during the study; or if they had an intolerance to caffeine and/or other natural stimulants. Exception was given to participants whose primary physician believed the condition or history to be controlled and thus not a limiting factor to their involvement. In which case, we required their physician complete a *Physician Clearance form* (Appendix F), allowing them to return. Ineligible parties were kept on file, as prospects, for potential entry into similar future studies, unless they objected.

Independent and Dependent Variables

The target variables measured as study outcomes are inclusive of; body weight [*primary outcome*]; followed by body composition (i.e. fat/fat-free mass, and fat percent) and anthropometric measurements (i.e. BMI and waist-to-hip ratio), blood chemistry measures (i.e. ALP, AST, ALT, creatinine, BUN, CK, LDH, glucose, total cholesterol, HDL, LDL, triglycerides, and whole blood complete blood count with platelet differential), hunger and satiety questionnaires, resting energy expenditure (indirect calorimetry), and diet characteristics [*secondary outcomes*]; lastly, cardiometabolic syndrome risk factors (i.e. body composition, blood pressure, serum glucose, Insulin, HOMA-IR, and lipoproteins) expressed as a summated z-score, physical activity, side effects, and sleep effects [*tertiary outcomes*]. These study outcomes serve as dependent variables, while the supplement interventions act as independent variables.

Familiarization Session

At the familiarization (FAM/T1) participants received printed and verbal explanations of the study design, protocols, procedures, equipment, and blood measures, lastly, a tour of the facility and testing areas. *Informed Consent forms* (Appendix D) were read and signed, personal/medical histories taken, and anthropometric measurements assessed (height, weight, BMI, blood pressure, and heart rate). Participants completed a *General Health Screening form* (Appendix E), reviewed by a registered nurse, whom if indicated, assessed fasting blood to rule out diabetes. Additionally, participants were shown and given instructions on dietary logs and activity trackers; trackers were worn 5 consecutive days (3 week, 2 weekend; Weds-Sun/Sun-Weds) and returned at baseline.

Testing Protocol

Participants were to refrain from exercise 48 hours prior to each testing session and be approximately 12 hours fasted. Upon arrival, on day one, activity trackers had been collected to calculate average step count for a five-day period and to assess if it met our goal activity range (5,000 to 9,999 steps/d). If so, baseline testing proceeded; if not, the individual discontinued the study. Participants meeting criteria were randomly assigned to a placebo-control group (6g dextrose, PLA) or one of two weight loss supplement groups (Figure 1); with caffeine (WL+C *A.M.* 125 mg | *P.M.* 150 mg) or without caffeine (WL), balancing for BMI, body fat percent, step count, sex, and age.

Stimulant Formula (WL+C)

AM Dose	
Dietary Ingredient	**(mg/dose)**
XR Caffeine (77% Caffeine)	150
Sensoril	125
Caffeine Anhydrous 98.5%	100
Capsimax™ Capsicum Extract 4% Capsaicinoids	25
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	250
Magnesium Stearate	14
Total Quantity	**784**

PM Dose	
Dietary Ingredient	**(mg/dose)**
DygloFit™ Dichrostachys glomerata extract	300
Caffeine Anhydrous 98.5%	150
Capsimax™ Capsicum Extract 4% Capsaicinoids	25
Clubmoss Ext 1% Huperzine	10
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	230
Magnesium Stearate	15
Total Quantity	**850**

Non-Stimulant Formula (WL)

AM Dose	
Dietary Ingredient	**(mg/dose)**
Sensoril® Ashwaganda (Withania somnifera)	250
Bioperine	5
Capsimax® Cayenne (Capsicum annuum) fruit extract (4% Capsaicinoids)	25
Rhodiola rosea extract	60
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	250
Magnesium Stearate	14
Total Quantity	**724**

PM Dose	
Dietary Ingredient	**(mg/dose)**
DygloFit™ Dichrostachys glomerata extract	300
Capsimax® Cayenne (Capsicum annuum) fruit extract (4% Capsaicinoids)	25
L-Theanine	100
Toothed clubmoss (Huperzia serrata) aerial parts extract (1% Huperzine A)	5
Bacopa monneri extract	50
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	230
Magnesium Stearate	15
Total Quantity	**845**

Figure 1. ***Study Formulas.***

During baseline (T2) and subsequent sessions (T3, T4, and T5), measures of body weight was collected first, followed by a review of the diet log. Then we measured, Resting Energy Expenditure (REE), body composition (DEXA), with a radiation exposure questionnaire filled out prior, body water (BIA), heart rate, and blood pressure. Afterward, BMI was calculated, and waist and hip circumference was measured. At this point questionnaires were administered including; a physical activity questionnaire, eating satisfaction survey, sleep index, and side effects inventory. Lastly, participants donated blood (≈ 20 ml), using standard venipuncture techniques, from the median cubital vein in the antecubital fossa of the arm. The remaining sessions (T3, T4, and T5) had been scheduled 28-40 days apart. Each participant also needed to retrieve an activity tracker about one week prior to the final session and wear it for another 5 consecutive days (3 week; 2 weekend days), returned at the final visit to calculate the final average step count. Figure 2 offers an overview of the study protocol and timeline.

Supplementation Protocol

Supplements were double-blind, having been packaged and bottled, with no content indicators. The bottles were plain, white, and labeled A, B, or C with an A.M. or P.M. designator. Participants received two bottles (A.M.; P.M.) of their respective supplement after each session, with a 40-day supply. Supplement consumption was twice a day, one capsule in the morning from the A.M. bottle and one in the afternoon from the P.M. bottle; suggested 7:00-9:00 a.m. and 2:00-4:00 p.m. or a minimum 5 hours, but less than 9 hours, between A.M. and P.M. doses. ESNL staff counted the remaining pills at following visits, ensuring compliance, and distributing more.

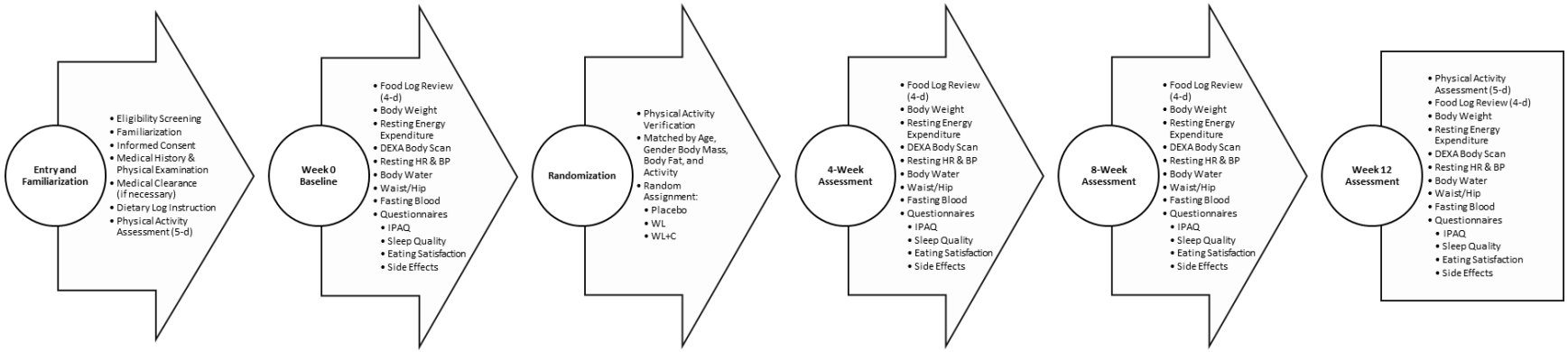

Figure 2. ***Study Protocol.*** *Overview of the study timeline and testing procedures in the order they were performed. Week 0/Baseline (T1) and Randomization occurred simultaneously, followed by Week 4 (T2); Week 8 (T3); and Week 12 (T5) as the final assessment.*

Testing Methodologies

Food Intake

Dietary records (*Food Logs*; Appendix I) were used to assess general intake prior to baseline and between visits, totaling four. Instruction, ongoing support, and review for reporting food intake was performed by a certified chef, trained in clinical dietetics. Each record detailed any four days, consecutive or not, of usual intake (3 week; 1 weekend) on non-testing days. Dietary records were input and analyzed using the Food Processor Nutrition Analysis Software, Version 11.3.285 (*ESHA Nutrition Research, Salem, OR*).

Physical Activity

The *International Physical Activity Questionnaire* (IPAQ; Appendix J) is a globally validated surveying tool for adults age 15-69, using set domains, over a 7-day period.[183-185] The "short-form" iteration of the IPAQ was used, comprised of 7 questions, in 4 domains (leisure-, domestic-, occupational-, transportation-related), aimed at 3 activity types (walking, moderate and vigorous intensity). Question responses provided frequency and duration of each activity type, which was gauged by its metabolic equivalents (METs), producing weekly averages (MET min) for each type. In addition, one question concerning time spent sitting was omitted, as per IPAQ scoring protocol.

Body Composition

Bone mineral density and body composition (fat mass; fat-free mass; lean mass; percent fat) was gathered by means of dual energy x-ray absorptiometry (DEXA; *Hologic Inc, Waltham, MA, USA*) scan, with APEX Software (*APEX Corporation Software, Pittsburg, PA, USA*), determining tissue density with low-dose x-ray radiation.[186,187]

Hence, participants completed a *Radiation Consent form* (Appendix G) prior to each scan. Quality Control (QC) calibrations were done on testing days by scanning a phantom spine (*Discovery W-Caliber Model DPA/QDR-1*). Each scan gives 1.5 mRs of whole-body radiation exposure over 6 minutes, totaling 6 mRs (4 scans) for 12 weeks. Our labs test-retest reliability studies on male athletes, repeated days, show a C_V range of 0.31-0.45% for total bone mineral content and fat-free mass with a mean intraclass correlation (ICC) of 0.98. Cranium data was excluded from the analysis.

Total Body Water

Total body water was determined with an ImpediMed SFB7 bioelectrical impedance analyzer (BIA; *ImpediMed, San Diego, CA, USA*), which uses a weak electric current to approximate body composition and water content based on how, and to what degree, conduction is affected by various tissue densities. Measurements were performed in a supine position, with two electrodes placed on the dorsal side of the hand and two on the dorsal side of the foot, lasting 10-15 seconds. BIA has shown to be a valid method of determining total body water.[188,189] Test-retest reliability from this lab yield an SEM of 0.75 and 0.02% of grand mean, C_V range of 0.23-0.26, and an ICC range of 0.94-0.98, consistent with previous studies.[190-192]

Anthropometry

Body mass (kg) and height (cm) were evaluated on a Health-O-Meter Professional 500KL (*Pelstar LLC, Alsip, IL, USA*) self-calibrating digital scale (±0.02 kg). Waist and hip circumference (cm) measures used standard measuring tape, as per ACSM's Guidelines for Exercise Testing and Prescription.[193] Both rounded to the nearest tenth or hundredth.

Resting Energy Expenditure

Resting Energy Expenditure (REE) measures used an open-circuit method of indirect calorimetry with the ParvoMedics TrueMax 2400 Metabolic Measurement System (Parvomedics Inc, Sandy, UT). At the start of each testing session day, quality control (QC) procedures were performed for gas and flowmeter calibration. The gas analyzer was calibrated against known concentrations, and the flowmeter with the Hans Rudolph series 5530 three-liter syringe (Hans Rudolph Inc., Kansas City, MO) following standard procedures. Per manufacturer, the coefficient of variation (C_V) used for apparently healthy individuals is ±2%. For testing, the participant remained supine for approximately 30 minutes, occasionally longer if measurements were not stable enough, with a plastic dome (hood) covering their head and plastic sheet covering the upper body, preventing external air entry, while their legs remained elevated on a foam box. The participants were asked to relax and stay awake during the procedure, and informed that a lab technician would check in regularly. Resting pulmonary exchange was measured, whereby expiration passively diffused from the hood, through tubing; to a metabolic cart measuring gas exchange (i.e. [VO_2] O_2 consumed ↔ [VCO_2] CO_2 expired) by comparing inspired and expired concentrations of O_2 and CO_2 from air within the hood. Data output every minute was utilized by averaging five consecutive time points varying the least (<5%) in rate of VO_2 and VCO_2, after the first ten minutes, for principle variables of interest (i.e. VO_2 L/min; REE kcal/d; RQ [VCO_2/VO_2]).[194,195] Percent glucose and fatty acid utilization was calculated via nonprotein RQ equation (Appendix A).[196]

Blood Collection

Participants donated roughly 20 mL of (8-12 hrs) fasted blood from the median cubital vein in the antecubital fossa of the arm, at each testing session. Whole blood was collected at the end of every visit, into two 7.5 mL BD Vacutainer® serum separation tubes and one 3.5 mL BD Vacutainer® K2 EDTA tube (*Becton, Dickinson and Company, Franklin Lakes, New Jersey*). Tubes sat at room temperature for 15-minutes, afterwards the 7.5 mL tubes were centrifuged, 3500 rpm for 10-minutes, in a refrigerated (4°C) bench top Thermo Scientific Heraeus MegaFuge 40R Centrifuge (*Thermo Electron North America LLC, West Palm Beach, FL, USA*). Tubes were kept at 4°C for 3-4 hours before analysis or storage. Serum was stored at -80°C, in polypropylene microcentrifuge tubes.

Blood Chemistry

Serum. Samples were analyzed for the following: alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT), creatinine, blood urea nitrogen (BUN), creatine kinase (CK), lactate dehydrogenase (LDH), glucose, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL; calculated), and triglycerides (TG) using a Cobas® c111 (*Roche Diagnostics, Basel, Switzerland*) automated clinical chemistry analyzer. Calibration of the analyzer was run daily, per manufacturer guidelines, and is known to be valid and reliable from previously published reports.[197] Internal QC uses two levels of control fluids, from the manufacturer, to calibrate acceptable standard deviation (SD) and C_V values for all assays. Samples were re-run if the values observed fell outside control values and/or clinical averages, according to standard procedures. In our lab, prior analysis has yielded a test-to-test reliability C_V

ranging from 0.4-2.4% and 0.6–1.9% with precisions of 0.8-2.4% and 0.5–1.7% for low and high controls, respectively.

Additionally, fasting insulin and leptin were measured using a commercially available enzyme linked immunosorbent assay kit (ELISA; *ALPCO Diagnostics, Salem, NH*). A BioTek ELX-808 Ultramicoplate reader (*BioTek Instruments Inc, Winooski, VT*) was used with an optical density of 450 nm against known standard curves, following standard procedures from the BioTek Gen5 Analysis software. The intra-assay C_V has shown to range from 5.1-10.3%, and the inter-assay C_V ranges from 6.7-16.6%. The following equation; $\frac{\left(glucose\frac{mmol}{L}\right)\left(insulin\frac{\mu IU}{mL}\right)}{22.5}$ was used to calculate Homeostatic Model of Assessment for Insulin Resistance (HOMA-IR).[198]

Whole Blood. A complete blood count (CBC) with platelet differential (hemoglobin, hematocrit, red blood cell counts, mean corpuscular volume [MCV], mean corpuscle hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC], red blood cell distribution width [RDW], white blood cell counts, lymphocytes, granulocytes, and mid-range absolute count [MID]) was measured using an Abbott Cell-Dyn 1800 (*Abbott Laboratories, Abbott Park, IL, USA*) automated hematology analyzer. The internal QC was performed using three levels of control fluids, from the manufacturer, to calibrate acceptable SD and C_V values for whole blood cell parameters. Test-to-test reliability assessment of assays, evaluated in previous studies, have yielded mean C_V's $< \pm 6.3\%$ with r-values > 0.9.

Hemodynamic Assessment

Resting heart rate and blood pressure was assessed with the participant in a supine position. Heart rate was determined by palpating the radial or ulnar artery, with blood pressure being measured thereafter. Blood pressure assessment used standard stethoscopes and sphygnanometers, listening to Korotkoff sounds, from the brachial artery, in the antecubital region of the elbow.[199,200]

Psychosocial Evaluation

A battery of questionnaires were utilized for the purpose of evaluating physical activity (described previously), general feelings of hunger and satiety, individual quality of sleep, and self-reported side effects between testing days. Instructions were provided on each document.

Hunger/Satiety. The *Eating Satisfaction Survey* (Appendix K), developed by the ESNL for Curves®, used a visual analogue scale (VAS) to rate severity of diet related symptoms (0; none, 10; severe) such as, appetite, hunger, satisfaction from food, fullness, energy, and overall diet quality. This survey has been used in similarly designed studies from our lab along with being published and deemed as a valid tool.[201] Day-to-day variability, in our lab, has shown an SEM of 0.07 and 0.01% of grand mean, C_V range of 0.16-0.29, and ICC range 0.73-0.86.

Sleep Quality. A *Sleep Quality Index* (SQI; Appendix L) was also administered at each visit, to determine the tolerability and potential sleep related symptoms of supplementation. The SQI is an effective device in evaluating quality and patterns of sleep; discerning "poor" from "good" sleep quality by inspecting sleep duration, sleep quality,

enthusiasm, and sleep disturbances of the past 48 hours. Furthermore, it possesses a 10-item "yes" or "no" question addressing sleep troubles including; falling asleep within 30 minutes, waking sporadically, frequent bathroom use, breathing complications, feeling cold or hot, bad dreams, pain, and any others. Day-to-day variability, in our lab, has shown an SEM of 0.38 and 8.2% of grand mean, C_V range of 0.22-2.2, and an ICC range of -1.3-0.92.

Side Effects. The *Weekly Follow-Up Assessment* (Appendix M) documented how well the supplements were tolerated, or perceived, and help monitor adherence to the protocol. Assessment was administered at baseline (T2) and weeks 4 (T3), 8 (T4), and 12 (T5); collecting reported symptoms of dizziness, headache, tachycardia, heart skipping or palpitations, shortness of breath, nervousness, blurred vision, and any other adverse effects. Participants were asked to rate the frequency and severity of their symptoms, respectively, using 0 (none), 1 (minimal 1-2/wk), 2 (slight 3-4/wk), 3 (occasional 5-6/wk; moderate), 4 (frequent 7-8/wk; severe), or 5 (severe ≥ 9/wk; very severe).

Statistical Analysis

All statistical analysis were performed with IBM SPSS® 25.0 (*IBM Statistics, Chicago, IL; IBM Corp., Armonk, NY, USA*). Data analysis used general linear models (GLM), with repeated measures, multivariate analysis of variance (MANOVA). The sample size was determined based on the expectation of a 5% improvement in weight loss with corresponding power of 0.80. Baseline demographic data analysis used one-way analysis of variance (ANOVA). Delta (Δ) change values were calculated and used to determine changes from baseline. Overall multivariate effects are expressed through

Wilks' Lambda distributions. Greenhouse-Geisser univariate tests of within-subjects; time (T), group x time (GxT), sex x time (SxT), and group x sex x time (GxSxT) effects and between-subjects; group (G), sex (S), and group x sex (GxS) effects are reported for each variable analyzed, to control for sphericity. For hematologic assessment, blood chemistry measurements were weighed relative to normal clinical limits, where the frequency in which a variable deviated outside of normal clinical limits, from baseline to 12 weeks, using a Chi-square analysis for each group as follows: (1) normal at baseline and week 12, (2) normal at baseline, high at week 12, (3) high at baseline, normal at week 12, (4) high at baseline and week 12. Data was considered statistically significant when the probability of type I error (α-level) is ≤0.05 with trends noted when the probability of error (p-level) range is 0.05-0.10 ($0.05< p <0.10$). If a significant treatment and/or interaction α-level was observed, Fisher's least significant difference post-hoc analysis was performed to determine where significance was obtained. When a non-significant treatment and/or interaction α-level was observed, analyses of mean change from baseline with 95% CI and Sidak adjustment, was performed. Partial Eta squared effect sizes (η_p^2) are reported as an indicator of effect size. Mean changes with 95% CI's completely above or below baseline were considered significantly different.[202] Missing data was extrapolated from the average of one time point immediately before and after; for week 12 (T5), the last observed value was carried forward (LOCF). Data is presented as mean ± SD and mean change ± 95% CI as appropriate. Data in figures include Δ-change from baseline and/or mean ± SD.

CHAPTER IV

RESULTS

Study Participants

Ninety-two participants were initially recruited for this study, wherein they completed a familiarization session and signed a consent form. Of the original 92 participants, 11 of them dropped, or were dropped, from the study prior to baseline, because 2 participants did not meet the activity criteria (average steps per day), 2 participants had scheduling conflicts, 1 participant had a family complication arise, and 6 participants gave no reason and/or were unable to be contacted. The remaining 81 individuals, 33 men (M) and 48 women (F), completed a baseline session and were then randomized into groups, allocating 27 (M 11; F 16) to the placebo (PLA), 24 (M 10; F 14) to the weight loss supplement (WL), and 30 (M 12; F 18) to the weight loss supplement with caffeine (WL+C) groups. Of these 81, 13 participants dropped, or were dropped, throughout the course of the study; 5 were due to reported side effects, 4 did not follow the supplementation protocol, 2 had scheduling conflicts, and 2 were unable to be contacted. Sixty-eight men (N=31) and women (N=37) completed the 12-week intervention, with group totals of; 22 (M 10; F 12) participants in PLA, 23 (M 10; F 13) participants in WL, and 23 (M 11; F 12) participants in WL+C. *Figure 3* represents a Consolidated Standards of Reporting Trials (CONSORT) diagram for study participants. This investigation was performed in accordance with the Declaration of Helsinki and approved by the Texas A&M University Institutional Review Board (#2016-0829FX).

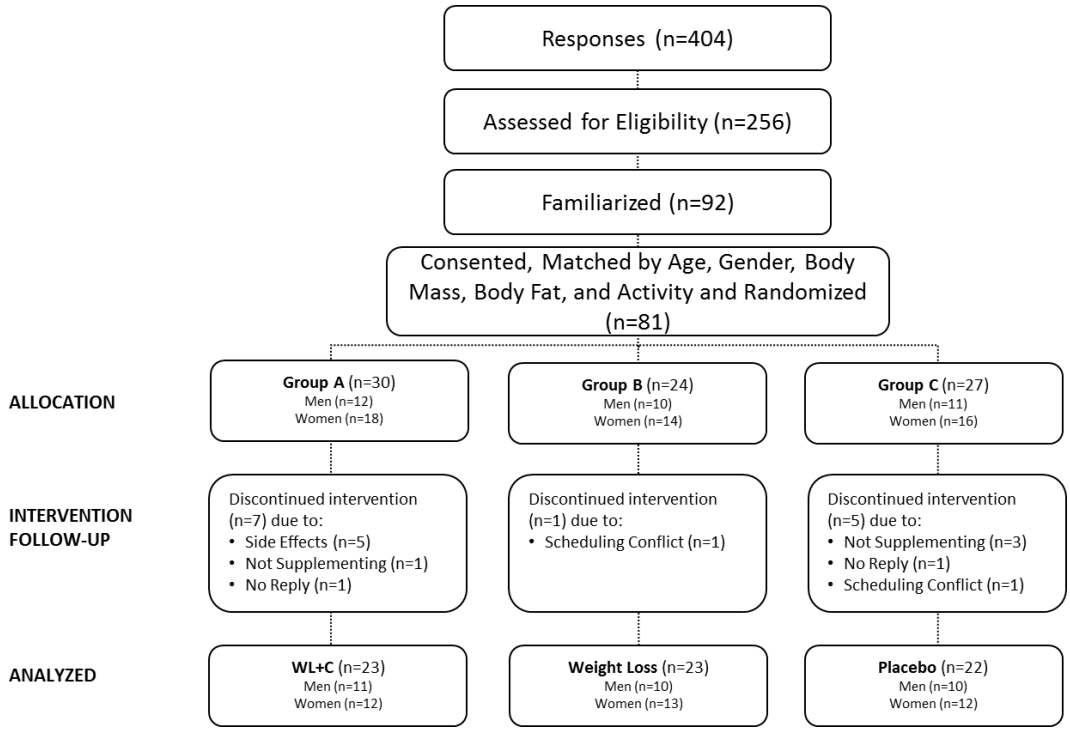

Figure 3. ***CONSORT Diagram.***

Baseline Characteristics

Univariate analysis revealed no significant differences between groups for age (37±5 yrs), height (170.5±11.3 cm), weight (88.9±16.6 kg), BMI (30.4±3.3 kg/m^2), body fat (35.2±7.7%), or activity (6,857±1,512 steps/wk). Pairwise analysis showed significant interaction effects of sex ($p<0.001$) with males being taller (M 179.8±9.5; F 162.7±4.9 cm) and weighing more (M 98.9±16.4; F 80.4±11.3 kg) overall, but females had greater body fat (M 28.3±4.9; F 40.9±3.9%), for all groups. Initial body fat ranged 18.6-47.4% (same in PLA), 22.3-46.6% in WL+C, and 21.6-46% in WL. Lastly, were generally more active (M 7,739±1,521; F 6,087±768 steps/wk) than females, in PLA. Yet, females in WL were more active than in other groups (WL 6,303±1,375; PLA 6,087±768; WL+C 7,595±1,707 steps/wk). *Table 4* presents participant baseline characteristics.

Table 4: Baseline Characteristics

Variable		Group PLA	Group WL	Group WL+C	Overall Mean	Effect	p-Level	η_p^2
Age		37 ± 5	37 ± 5	37 ± 4	37 ± 5	Group	0.93	0.002
(years)	F	38 ± 5	36 ± 5	36 ± 4	36 ± 5	Sex	0.24	0.02
	M	37 ± 4	38 ± 6	39 ± 4	38 ± 5	G x S	0.28	0.04
Weight		90.52 ± 17.55	88.58 ± 14.99	87.54 ± 17.72	88.86 ± 16.58	Group	0.70	0.01
(kg)	F	80.23 ± 12.70 ♂	82.22 ± 12.34 ♂	78.61 ± 8.97 ♂	80.40 ± 11.26 ♂	Sex	<0.001	0.32
	M	102.87 ± 14.53 ♂	96.84 ± 14.56 ♂	97.29 ± 20.06 ♂	98.95 ± 16.39 ♂	G x S	0.64	0.01
Height		171.51 ± 13.71	170.95 ± 10.48	169.16 ± 9.65	170.53 ± 11.25	Group	0.33	0.04
(cm)	F	161.58 ± 4.25 ♂	164.02 ± 6.41 ♂	162.53 ± 3.58 ♂	162.74 ± 4.91 ♂	Sex	<0.001	0.60
	M	183.43 ± 11.27 c♂	179.97 ± 7.34 ♂	176.40 ± 8.97 a♂	179.82 ± 9.47 ♂	G x S	0.17	0.05
BMI		30.64 ± 3.41	30.17 ± 3.32	30.51 ± 3.23	30.44 ± 3.27	Group	0.86	0.005
(kg/m^2)	F	30.67 ± 3.86	30.49 ± 3.39	29.73 ± 2.60	30.30 ± 3.26	Sex	0.74	0.002
	M	30.59 ± 3.00	29.74 ± 3.35	31.37 ± 3.74	30.59 ± 3.34	G x S	0.47	0.02
Body Fat		35.49 ± 8.16	34.69 ± 7.64	35.38 ± 7.71	35.18 ± 7.72	Group	0.58	0.02
(%)	F	41.53 ± 4.15 ♂	40.46 ± 3.70 ♂	41.00 ± 4.03 ♂	40.98 ± 3.87 ♂	Sex	<0.001	0.69
	M	28.24 ± 5.23 ♂	27.18 ± 3.69 ♂	29.25 ± 5.78 ♂	28.25 ± 4.92 ♂	G x S	0.80	0.007
Activity		6,838 ± 1,417	7,198 ± 1,548	6,534 ± 1,554	6,857 ± 1,512	Group	0.37	0.03
(Steps/wk)	F	6,087 ± 768 b♂	7,595 ± 1,707 ac	6,303 ± 1,375 b	6,687 ± 1,482	Sex	0.25	0.02
	M	7,739 ± 1,521 ♂	6,683 ± 1,204	6,785 ± 1,760	7,060 ± 1,546	G x S	0.02	0.13

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.97), Sex (p<0.01), and Group x Sex (p=0.15) effects for baseline demographic variables. Univariate p-levels are listed for Group (G), Sex (S), and Group x Sex (G x S) interaction effects. Pairwise comparison is indicated by the following superscripts: ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C.

Energy Utilization and Body Measurements

Energy and Macronutrient Intake

Repeated measures MANOVA analyses revealed overall Wilks' Lambda Sex (p<0.01) and Time (p=0.09) effects, with no significant Group (p=0.22), Group x Time (p=0.13), Sex x Time (p=0.27), Group x Sex (p=0.47), or Group x Time x Sex (p=0.64) effects for the energy and macronutrient variables, calories (kcal/d), protein (g/d), carbohydrate (g/d), and total fat (g/d). Greenhouse-Geisser univariate analysis showed significant effects of sex (p<0.01) for all measures; of time (p<0.05) for calories and protein; also of group x sex (p<0.05) for fat. Conversely, no group x time, sex x time, or group x time x sex effects were seen among intake variables. Pairwise analysis showed supplement groups (WL+C and WL) did not significantly differ from each other but, were consistently lower than PLA at all time points and measures of intake. Protein intake was

significantly lower than PLA in WL at week 8 (PLA 82.6±29.7; WL 69.2±26.3 g/d) and in both supplement groups at week 12 (PLA 82.1±30.2; WL 67.3±23.7; WL+C 69.0±22.6 g/d). Furthermore, carbohydrate intake significantly decreased in PLA from baseline to week 12 (PLA 206.6±93.0; PLA 171.9±80.9 g/d), as did fat intake in WL (WL 67.7±27.9; WL 52.8±19.4 g/d). In addition, males overall had greater intake of calories (F 1,488±73; M 2,018±80 kcal/d), protein (F 63.8±2.9; M 91.9±3.2 g/d), carbohydrates (F 161.8±8.9; M 206.1±9.7 g/d), and fat (F 58.1±3.4; M 77.2±3.7 g/d). *Table 5* presents energy and macronutrient intake within each group. These data fail to reject $H_0$5: Diet characteristics in treatment groups will not significantly differ from baseline and/or placebo.

Physical Activity

Overall Wilks' Lambda revealed no significant Group (p=0.34), Time (p=0.84), Group x Time (p=0.98), Sex (p=0.29), Sex x Time (p=0.97), Group x Sex (p=0.70), or Group x Time x Sex (p=0.92) effects on physical activity variables, walking, moderate, vigorous, and total activity (MET/min). Univariate analysis indicated no interaction effects among physical activity variables as well. Pairwise analysis showed no significant differences among treatments. Pairwise analysis of truncated IPAQ data indicated a drop in baseline reported walking for WL by week 4 (WL 1,775±1,412; WL 1,225±1,286 MET min) and an increase by week 12 for females of WL+C (WL+C 1,247±1,323; WL+C 2,278±1,806 MET/min). Otherwise, results were similar to analysis of non-truncated data. *Tables 6-6.1* present the International Physical Activity Questionnaire (IPAQ) and truncated results, respectively, within each group.

Table 5: Energy and Macronutrient Intake

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Calories (Kcals/d)	PLA		2,047 ± 706 [c]	1,846 ± 587 [†]	1,843 ± 623	1,835 ± 749 [c]	1,927 ± 95 [c]	Group	0.07	0.08
	WL		1,748 ± 568	1,676 ± 545	1,640 ± 615	1,573 ± 467	1,702 ± 93	Time	0.02	0.05
	WL+C		1,674 ± 561 [a]	1,665 ± 578	1,631 ± 518	1,534 ± 534 [a]	1,630 ± 92 [a]	G x T	0.74	0.02
	Time		1,820 ± 626	1,728 ± 568	1,703 ± 586	1,645 ± 599 [†]				
	F		1,615 ± 438 [♂]	1,521 ± 414 [♂]	1,421 ± 327 [†♂]	1,384 ± 398 [†♂]	1,488 ± 73 [♂]	Sex	<0.001	0.28
	M		2,064 ± 729 [♂]	1,974 ± 631 [♂]	2,039 ± 650 [♂]	1,955 ± 654 [♂]	2,018 ± 80 [♂]	S x T	0.31	0.02
	PLA	F	1,666 ± 353 [♂]	1,610 ± 230 [♂]	1,518 ± 221 [♂]	1,420 ± 292 [♂]	1,553 ± 128 [♂]	G x S	0.09	0.08
		M	2,505 ± 765 [c♂]	2,130 ± 759 [†♂]	2,234 ± 731 [♂]	2,334 ± 835 [c♂]	2,301 ± 140 [c♂]	G x T x S	0.30	0.04
	WL	F	1,514 ± 383 [♂]	1,376 ± 412 [♂]	1,298 ± 343 [♂]	1,316 ± 337 [♂]	1,376 ± 123 [♂]			
		M	2,054 ± 641 [♂]	2,067 ± 448 [♂]	2,084 ± 615 [♂]	1,906 ± 403 [♂]	2,028 ± 140 [♂]			
	WL+C	F	1,674 ± 569	1,588 ± 532	1,457 ± 379	1,422 ± 549	1,535 ± 128			
		M	1,674 ± 579 [a]	1,749 ± 638	1,821 ± 597	1,656 ± 513 [a]	1,725 ± 133 [a]			
Protein (g/d)	PLA		89.5 ± 31.2	81.8 ± 26.4	82.6 ± 29.7 [b]	82.1 ± 30.2 [bc]	85.8 ± 3.8 [b]	Group	0.04	0.10
	WL		78.2 ± 34.0	70.2 ± 27.2	69.2 ± 26.3 [a]	67.3 ± 23.7 [a]	73.3 ± 3.8 [a]	Time	0.01	0.06
	WL+C		79.6 ± 29.4	72.8 ± 23.6	75.2 ± 22.1	69.0 ± 22.6 [a]	74.4 ± 3.7	G x T	0.97	0.01
	Time		82.3 ± 31.6	74.9 ± 25.8 [†]	75.6 ± 26.4 [†]	72.7 ± 26.1 [†]				
	F		69.4 ± 22.0 [♂]	63.8 ± 17.7 [♂]	62.8 ± 17.9 [♂]	58.6 ± 17.2 [†♂]	63.8 ± 2.9 [♂]	Sex	<0.001	0.40
	M		97.8 ± 34.4 [♂]	88.1 ± 28.0 [†♂]	90.8 ± 26.9 [♂]	89.5 ± 25.1 [♂]	91.9 ± 3.2 [♂]	S x T	0.69	0.01
	PLA	F	66.8 ± 15.1 [♂]	69.5 ± 14.1 [♂]	64.3 ± 8.5 [♂]	64.1 ± 18.5 [♂]	66.2 ± 5.2 [♂]	G x S	0.05	0.09
		M	116.9 ± 21.9 [c♂]	96.6 ± 30.6 [†♂]	104.5 ± 31.6 [c♂]	103.8 ± 27.3 [c♂]	105.4 ± 5.7 [bc♂]	G x T x S	0.49	0.03
	WL	F	66.3 ± 23.4 [♂]	55.7 ± 15.6 [♂]	55.5 ± 20.6 [♂]	52.5 ± 13.1 [♂]	57.5 ± 5.0 [♂]			
		M	93.6 ± 40.3 [♂]	89.1 ± 28.0 [♂]	87.1 ± 22.5 [♂]	86.7 ± 20.3 [♂]	89.1 ± 5.7 [a♂]			
	WL+C	F	75.2 ± 26.6	66.8 ± 20.9	69.1 ± 20.3	59.9 ± 19.0 [♂]	67.7 ± 5.2			
		M	84.3 ± 32.8 [a]	79.5 ± 25.5	81.9 ± 23.0 [a]	79.0 ± 22.7 [a♂]	81.1 ± 5.4 [a]			
Carbohydrate (g/d)	PLA		206.6 ± 93.0	188.1 ± 66.3	185.6 ± 57.6	171.9 ± 80.9 [†]	190.7 ± 11.5	Group	0.28	0.04
	WL		204.2 ± 77.6	185.1 ± 68.7	176.5 ± 70.5	188.3 ± 62.4	192.0 ± 11.3	Time	0.06	0.04
	WL+C		171.9 ± 64.2	172.1 ± 68.9	171.9 ± 64.9	158.7 ± 60.0	169.2 ± 11.2	G x T	0.65	0.02
	Time		194.1 ± 79.4	181.7 ± 67.3	177.9 ± 64.0	173.0 ± 68.3 [†]				
	F		176.1 ± 69.5 [♂]	166.3 ± 55.7 [♂]	153.7 ± 51.6 [♂]	151.5 ± 59.0 [†♂]	161.8 ± 8.9 [♂]	Sex	<0.01	0.16
	M		215.5 ± 86.0 [♂]	200.1 ± 75.9 [♂]	206.8 ± 66.0 [♂]	198.7 ± 70.6 [♂]	206.1 ± 9.7 [♂]	S x T	0.63	0.01
	PLA	F	179.4 ± 78.2	171.1 ± 35.3	166.9 ± 38.3	128.5 ± 44.7 [†‡♂]	161.5 ± 15.5 [♂]	G x S	0.48	0.02
		M	239.1 ± 103 [c]	208.6 ± 88.7	208.0 ± 70.2	224.1 ± 85.3 [c♂]	219.9 ± 17.0 [♂]	G x T x S	0.14	0.05
	WL	F	176.2 ± 69.7 [♂]	166.9 ± 68.7	147.0 ± 53.9 [♂]	172.9 ± 56.1	165.7 ± 14.9 [♂]			
		M	240.7 ± 75.1 [c♂]	208.8 ± 64.3	214.8 ± 73.5 [♂]	208.5 ± 67.2	218.2 ± 17.0 [♂]			
	WL+C	F	172.7 ± 66.1	160.7 ± 60.7	147.6 ± 61.4 [♂]	151.5 ± 69.6	158.1 ± 15.5			
		M	171.1 ± 65.4 [ab]	184.5 ± 77.8	198.5 ± 60.3 [♂]	166.6 ± 49.5 [a]	180.2 ± 16.2			
Total Fat (g/d)	PLA		75.6 ± 32.7	73.1 ± 27.0	74.9 ± 33.8 [c]	76.9 ± 33.1 [bc]	76.5 ± 4.4 [b]	Group	0.06	0.09
	WL		67.7 ± 27.9	62.6 ± 25.9	62.1 ± 25.0	52.8 ± 19.4 [a†‡]	63.0 ± 4.4 [a]	Time	0.11	0.03
	WL+C		68.1 ± 29.0	64.1 ± 26.9	61.1 ± 22.0 [a]	60.3 ± 25.9 [a]	63.4 ± 4.3	G x T	0.35	0.04
	Time		70.4 ± 29.7	66.5 ± 26.6	65.9 ± 27.6	63.2 ± 28.1 [†]				
	F		60.9 ± 22.7 [♂]	60.3 ± 21.2 [♂]	54.8 ± 12.9 [♂]	55.4 ± 21.7 [♂]	58.1 ± 3.4 [♂]	Sex	<0.001	0.19
	M		81.7 ± 33.2 [♂]	73.9 ± 30.6 [♂]	79.1 ± 34.1 [♂]	72.4 ± 32.1 [♂]	77.2 ± 3.7 [♂]	S x T	0.28	0.02
	PLA	F	58.6 ± 11.7 [♂]	63.9 ± 13.6 [♂]	59.9 ± 11.1 [♂]	63.3 ± 19.6 [♂]	61.4 ± 6.0 [♂]	G x S	0.04	0.10
		M	95.9 ± 38.5 [c♂]	84.2 ± 35.0 [c]	92.9 ± 43.0 [c♂]	93.3 ± 39.2 [bc♂]	91.6 ± 6.6 [c♂]	G x T x S	0.84	0.01
	WL	F	56.0 ± 16.3 [♂]	51.8 ± 19.5 [♂]	47.1 ± 12.4 [♂]	44.6 ± 14.1	49.9 ± 5.8 [♂]			
		M	83.0 ± 33.1 [♂]	76.7 ± 27.2 [♂]	81.6 ± 24.0 [♂]	63.6 ± 20.6 [a†‡]	76.2 ± 6.6 [♂]			
	WL+C	F	68.4 ± 34.1	65.8 ± 27.2	58.0 ± 12.1	59.3 ± 26.8	49.9 ± 6.0			
		M	67.7 ± 23.9 [a]	62.1 ± 27.7 [a]	64.4 ± 29.6 [a]	61.5 ± 26.2 [a]	63.9 ± 6.3 [a]			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.22), Time (p=0.09), Group x Time (p=0.13), Sex (p<0.01), Sex x Time (p=0.27), and Group x Sex (p=0.47), Group x Time x Sex (p=0.64) effects for energy and macronutrient variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 6: International Physical Activity Questionnaire (IPAQ) Results

			Weeks				Mean			
	Group		**0**	**4**	**8**	**12**	**(SEM)**	**Effect**	**p-Level**	η_p^2
Walking	PLA		925 ± 1,158 [b]	1,527 ± 2,506	1,145 ± 1,619	1,392 ± 1,473	1,217 ± 416	Group	0.40	0.03
MET Minutes	WL		2,498 ± 3,011 [a]	1,810 ± 3,139	1,679 ± 2,594	2,075 ± 3,310	1,965 ± 409	Time	0.86	0.003
	WL+C		1,586 ± 2,333	1,837 ± 2,675	1,971 ± 3,080	2,024 ± 2,203	1,834 ± 405	G x T	0.69	0.02
	Time		1,681 ± 2,368	1,727 ± 2,752	1,605 ± 2,502	1,837 ± 2,443				
	F		1,929 ± 2946	2,007 ± 3420	2,132 ± 3188	2,241 ± 2897	2,069 ± 320	Sex	0.10	0.04
	M		1,384 ± 1392	1,394 ± 1634	976 ± 1020	1,354 ± 1677	1,274 ± 349	S x T	0.73	0.01
	PLA	F	1,001 ± 1399 [b]	2,096 ± 3267	1,543 ± 2107	1,558 ± 1609	1,549 ± 561	G x S	0.97	<0.001
		M	833 ± 847	845 ± 815	668 ± 478	1,193 ± 1348	885 ± 614	G x T x S	0.81	0.01
	WL	F	2,881 ± 3708 [a]	1,929 ± 3806	2,274 ± 3293	2,335 ± 3925	2,355 ± 539			
		M	2,000 ± 1830	1,655 ± 2174	904 ± 899	1,737 ± 2454	1,574 ± 614			
	WL+C	F	1,825 ± 3069	2,002 ± 3433	2,566 ± 4048	2,823 ± 2682	2,304 ± 561			
		M	1,326 ± 1213	1,656 ± 1646	1,322 ± 1398	1,152 ± 1079	1,364 ± 586			
Moderate	PLA		365 ± 304	529 ± 578	755 ± 1,139	435 ± 502	531 ± 205	Group	0.34	0.03
MET Minutes	WL		835 ± 1,116	1,059 ± 1,539	903 ± 1,092	1,024 ± 1,939	956 ± 202	Time	0.54	0.01
	WL+C		567 ± 1,040	955 ± 2,455	710 ± 1,888	638 ± 761	719 ± 200	G x T	0.92	0.01
	Time		592 ± 912	852 ± 1,707	789 ± 1,405	703 ± 1,251				
	F		607 ± 1053	872 ± 2156	677 ± 1157	593 ± 1417	680 ± 158	Sex	0.64	0.004
	M		574 ± 725	829 ± 962	924 ± 1664	834 ± 1026	791 ± 172	S x T	0.75	0.01
	PLA	F	290 ± 292	285 ± 291	690 ± 1347	396 ± 575	415 ± 277	G x S	0.93	0.002
		M	454 ± 310	822 ± 708	832 ± 893	482 ± 424	648 ± 303	G x T x S	0.43	0.03
	WL	F	817 ± 1183	1,089 ± 1775	1,025 ± 1401	871 ± 2273	950 ± 266			
		M	858 ± 1086	1,020 ± 1259	744 ± 499	1,224 ± 1491	962 ± 303			
	WL+C	F	697 ± 1358	1,223 ± 3336	287 ± 347	490 ± 674	674 ± 277			
		M	425 ± 559	662 ± 912	1,171 ± 2694	800 ± 849	765 ± 289			
Vigorous	PLA		829 ± 726	803 ± 851	658 ± 856	596 ± 770	737 ± 159	Group	0.20	0.05
MET Minutes	WL		1,205 ± 1,151 [c]	1,024 ± 1,089	1,236 ± 1,357	1,023 ± 1,266	1,128 ± 157 [c]	Time	0.53	0.01
	WL+C		557 ± 710 [b]	630 ± 851	965 ± 1,645	579 ± 1,112	673 ± 155 [b]	G x T	0.79	0.01
	Time		864 ± 916	819 ± 938	957 ± 1,334	735 ± 1,078				
	F		899 ± 980	766 ± 968	999 ± 1492	749 ± 1196	847 ± 122	Sex	0.99	<0.001
	M		822 ± 848	883 ± 914	907 ± 1138	717 ± 937	845 ± 134	S x T	0.87	0.003
	PLA	F	733 ± 613	642 ± 735	487 ± 647	410 ± 664	568 ± 215	G x S	0.20	0.05
		M	944 ± 863	996 ± 977	864 ± 1055	820 ± 863	906 ± 235	G x T x S	0.95	0.01
	WL	F	1,200 ± 1311	911 ± 1128	1,152 ± 1526	1,052 ± 1363	1,079 ± 206			
		M	1,212 ± 974 [c]	1,172 ± 1076	1,344 ± 1171	984 ± 1200	1,178 ± 235 [c]			
	WL+C	F	740 ± 853	733 ± 1046	1,347 ± 1971	760 ± 1406 ‡	895 ± 215			
		M	356 ± 475 [b]	516 ± 601	549 ± 1146	382 ± 681	451 ± 224 [b]			
Total	PLA		2,118 ± 1,341 [b]	2,859 ± 2,541	2,558 ± 2,535	2,423 ± 1,661	2,485 ± 558 [b]	Group	0.14	0.06
MET Minutes	WL		4,538 ± 3,663 [ac]	3,893 ± 4,367	3,817 ± 3,560	4,122 ± 4,498	4,049 ± 548 [a]	Time	0.92	0.002
	WL+C		2,710 ± 2,904 [b]	3,421 ± 3,607	3,645 ± 4,775	3,241 ± 2,629	3,226 ± 544	G x T	0.75	0.02
	Time		3,137 ± 2,969	3,399 ± 3,569	3,352 ± 3,738	3,275 ± 3,204				
	F		3,435 ± 3606	3,645 ± 4250	3,808 ± 4138	3,584 ± 3478	3,597 ± 428	Sex	0.28	0.02
	M		2,781 ± 1960	3,106 ± 2570	2,807 ± 3177	2,906 ± 2855	2,910 ± 468	S x T	0.94	0.002
	PLA	F	2,024 ± 1557 [b]	3,022 ± 3132	2,719 ± 3195	2,364 ± 1910	2,532 ± 752	G x S	0.74	0.01
		M	2,231 ± 1098	2,663 ± 1729	2,364 ± 1564	2,495 ± 1403	2,438 ± 824	G x T x S	0.97	0.01
	WL	F	4,898 ± 4473 [a]	3,929 ± 5046	4,451 ± 4459	4,258 ± 4792	4,384 ± 722			
		M	4,070 ± 2385	3,847 ± 3559	2,992 ± 1769	3,945 ± 4333	3,714 ± 824			
	WL+C	F	3,261 ± 3684	3,959 ± 4573	4,199 ± 4711	4,073 ± 2908	4,384 ± 752			
		M	2,108 ± 1692	2,834 ± 2212	3,042 ± 4997	2,334 ± 2043	2,579 ± 785			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.34), Time (p=0.84), Group x Time (p=0.98), Sex (p=0.29), Sex x Time (p=0.97), and Group x Sex (p=0.70), Group x Time x Sex (p=0.92) effects for physical activity variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 6.1: International Physical Activity Questionnaire (IPAQ) Results (Truncated)

			Weeks				Mean			
	Group		**0**	**4**	**8**	**12**	**(SEM)**	**Effect**	**p-Level**	η_p^2
Walking	PLA		893 ± 1,050 [b]	1,086 ± 1,166	997 ± 1,206	1,284 ± 1,291	1,045 ± 215	Group	0.36	0.03
MET Minutes	WL		1,775 ± 1,412 [a]	1,225 ± 1,286 †	1,257 ± 1,350	1,352 ± 1,360	1,394 ± 211	Time	0.44	0.01
	WL+C		1,285 ± 1,243	1,372 ± 1,184	1,398 ± 1,369	1,740 ± 1,578	1,442 ± 210	G x T	0.37	0.03
	Time		1,324 ± 1,280	1,229 ± 1,201	1,221 ± 1,303	1,461 ± 1,410				
	F		1,348 ± 1443	1,231 ± 1252	1,444 ± 1522	1,728 ± 1629	1,437 ± 165	Sex	0.10	0.04
	M		1,295 ± 1078	1,228 ± 1158	954 ± 936	1,143 ± 1031	1,150 ± 181	S x T	0.19	0.03
	PLA	F	943 ± 1230	1,287 ± 1399	1,271 ± 1553	1,558 ± 1609	1,265 ± 290	G x S	0.87	0.004
		M	833 ± 847	845 ± 815	668 ± 478	955 ± 709	825 ± 318	G x T x S	0.57	0.02
	WL	F	1,815 ± 1686	1,107 ± 1145 †	1,528 ± 1597	1,376 ± 1461	1,456 ± 279			
		M	1,723 ± 1039	1,378 ± 1499	904 ± 899	1,322 ± 1293	1,332 ± 318			
	WL+C	F	1,247 ± 1323	1,309 ± 1310	1,526 ± 1530	2,278 ± 1806 †‡	1,590 ± 290			
		M	1,326 ± 1213	1,440 ± 1090	1,259 ± 1228	1,152 ± 1079	1,294 ± 303			
Moderate	PLA		365 ± 304	529 ± 578	667 ± 880	435 ± 502	510 ± 154	Group	0.22	0.05
MET Minutes	WL		772 ± 987	976 ± 1,277	903 ± 1,092	795 ± 1,214	862 ± 151	Time	0.41	0.01
	WL+C		483 ± 710	631 ± 1,125	527 ± 1,036	638 ± 761	573 ± 150	G x T	0.91	0.01
	Time		543 ± 738	715 ± 1,045	699 ± 1,006	625 ± 880				
	F		555 ± 872	645 ± 1149	644 ± 1051	502 ± 925	579 ± 118	Sex	0.43	0.01
	M		528 ± 550	798 ± 918	765 ± 963	772 ± 815	718 ± 129	S x T	0.64	0.01
	PLA	F	290 ± 292	285 ± 291	590 ± 1019	396 ± 575	390 ± 208	G x S	0.87	0.004
		M	454 ± 310	822 ± 708	760 ± 722	482 ± 424	630 ± 227	G x T x S	0.40	0.03
	WL	F	817 ± 1183	960 ± 1339	1,025 ± 1401	612 ± 1349	853 ± 199			
		M	714 ± 714	996 ± 1262	744 ± 499	1,032 ± 1032	872 ± 227			
	WL+C	F	537 ± 847	663 ± 1421	287 ± 347	490 ± 674	494 ± 208			
		M	425 ± 559	596 ± 748	789 ± 1444	800 ± 849	653 ± 217			
Vigorous	PLA		829 ± 726	803 ± 851	658 ± 856	596 ± 770	737 ± 158	Group	0.11	0.07
MET Minutes	WL		1,163 ± 1,066 [c]	1,024 ± 1,089	1,173 ± 1,236	1,023 ± 1,266	1,105 ± 155	Time	0.57	0.01
	WL+C		557 ± 710 [b]	630 ± 851	965 ± 1,645	579 ± 1,112	673 ± 154	G x T	0.78	0.02
	Time		850 ± 876	819 ± 938	936 ± 1,290	735 ± 1,078				
	F		874 ± 910	766 ± 968	961 ± 1420	749 ± 1196	832 ± 121	Sex	0.94	<0.001
	M		822 ± 848	883 ± 914	907 ± 1138	717 ± 937	845 ± 133	S x T	0.90	0.002
	PLA	F	733 ± 613	642 ± 735	487 ± 647	410 ± 664	568 ± 213	G x S	0.20	0.05
		M	944 ± 863	996 ± 977	864 ± 1055	820 ± 863	906 ± 233	G x T x S	0.91	0.01
	WL	F	1,126 ± 1169	911 ± 1128	1,042 ± 1314	1,052 ± 1363	1,033 ± 205			
		M	1,212 ± 974 [c]	1,172 ± 1076	1,344 ± 1171	984 ± 1200	1,178 ± 233 [c]			
	WL+C	F	740 ± 853	733 ± 1046	1,347 ± 1971	760 ± 1406 ‡	895 ± 213			
		M	356 ± 475 [b]	516 ± 601	549 ± 1146	382 ± 681	451 ± 222 [b]			
Total	PLA		2,087 ± 1,255 [b]	2,418 ± 1,554	2,322 ± 2,020	2,315 ± 1,543	2,292 ± 376 [b]	Group	0.13	0.06
MET Minutes	WL		3,710 ± 2,349 [ac]	3,225 ± 2,755	3,333 ± 2,418	3,170 ± 2,727	3,362 ± 369 [a]	Time	0.95	0.001
	WL+C		2,325 ± 1,860 [b]	2,633 ± 1,888	2,890 ± 3,222	2,957 ± 2,154	2,689 ± 366	G x T	0.69	0.02
	Time		2,717 ± 1,991	2,763 ± 2,130	2,856 ± 2,604	2,821 ± 2,201				
	F		2,777 ± 2270	2,642 ± 2075	3,049 ± 2754	2,979 ± 2334	2,848 ± 289	Sex	0.28	0.02
	M		2,645 ± 1631	2,909 ± 2220	2,626 ± 2437	2,633 ± 2052	2,713 ± 315	S x T	0.57	0.01
	PLA	F	1,967 ± 1410 [b]	2,214 ± 1437	2,347 ± 2455	2,364 ± 1910	2,223 ± 506	G x S	0.76	0.01
		M	2,231 ± 1098	2,663 ± 1729	2,292 ± 1467	2,257 ± 1043	2,361 ± 555	G x T x S	0.94	0.01
	WL	F	3,758 ± 2828 [a]	2,978 ± 2584	3,594 ± 2863	3,040 ± 2823	3,343 ± 487			
		M	3,649 ± 1679	3,546 ± 3073	2,992 ± 1769	3,338 ± 2737	3,381 ± 555			
	WL+C	F	2,524 ± 2055	2,706 ± 2099	3,160 ± 2991	3,528 ± 2177	3,343 ± 506			
		M	2,108 ± 1692	2,553 ± 1728	2,597 ± 3580	2,334 ± 2043	2,398 ± 529			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.32), Time (p=0.49), Group x Time (p=0.89), Sex (p=0.27), Sex x Time (p=0.58), and Group x Sex (p=0.54), Group x Time x Sex (p=0.78) effects for truncated physical activity variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Body Composition and Anthropometrics

Body Composition. Multivariate analysis revealed overall Wilks' Lambda Time ($p=0.07$) and Sex ($p<0.01$), with no Group ($p=0.94$), Group x Time ($p=0.88$), Sex x Time ($p=0.67$), Group x Sex ($p=0.94$), or Group x Time x Sex ($p=0.99$) effects for body composition variables, body weight (kg), fat mass (FM; kg), fat free mass (FFM; kg), body fat (BF; %), and bone mineral content (BMC; g). Univariate analysis found significant effects of sex ($p\leq0.01$) but, not group, time, group x time, sex x time, group x sex, or group x time x sex interactions for any body composition measure. Pairwise analysis bore no differences amid groups at any time point. Conversely, males exhibited weight loss from baseline at week 4 in supplement groups WL (WL 96.84±14.56; WL 95.75±14.91 kg) and WL+C (WL+C 97.29±20.06; WL+C 96.13±19.26 kg). No other effects occurred for body weight (*Table 7*). Still, WL lost FM, by weeks 4 and 8 (WL 28.01±7.13; Wk4 27.44±6.92; Wk8 27.38±7.22 kg) and BF at weeks 8 and 12 (WL 34.69±7.64; W8 34.06±7.82; Wk12 33.9±7.58 %). Analysis of change from baseline [95% CI] (*Figures 4-6*) also showed FM loss at weeks 4 and 8 (WL -0.56±0.95 [-1.02, -0.14]; Wk8 -0.63±1.47 [-1.23, -0.02] kg) with BF at weeks 8 and 12 (WL -0.63±1.26 [-1.16, -0.10]; Wk12 -0.78±1.31 [-1.45, 0.07] %). Sex differences implied females weighed less (F 80.15±2.35; M 98.5±2.56 kg), with less FFM (F 43.46±1.34; M 64.86±1.46 kg) and BMC (F 1.69±0.06; M 2.4±0.07 g) thus, more FM (F 30.34±1.21; M 25.58±1.32 kg) and BF (F 40.73±0.75; M 28.01±0.82 %). These data both reject $H_0$1: Body weight will decrease; and fail to reject $H_0$2: Body composition will improve; significantly in treatment groups compared to baseline and/or placebo.

Table 7: Body Composition and Anthropometric Data

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Body Weight (kg)	PLA		90.52±17.55	90.21±17.54	90.27±18.19	90.22±18.87	91.33±3.05	Group	0.67	0.01
	WL		88.58±14.99	87.91±14.96	88.12±15.59	88.15±15.85	89.12±3.00	Time	0.20	0.03
	WL+C		87.54±17.72	86.95±17.03	86.91±17.07	87.06±17.08	87.51±2.98	G x T	0.97	0.003
	Time		88.86±16.58	88.33±16.34†	88.41±16.77	88.45±17.08				
	F		80.40±11.26♂	80.24±11.23♂	80.09±11.35♂	80.05±11.73♂	80.15±2.35♂	Sex	<0.001	0.31
	M		98.95±16.39♂	97.99±16.37†♂	98.33±16.92♂	98.48±17.19♂	98.50±2.56♂	S x T	0.42	0.01
	PLA	F	80.23±12.70♂	80.16±12.56♂	80.08±12.75♂	79.69±13.59♂	80.04±4.12♂	G x S	0.63	0.01
		M	102.87±14.53♂	102.27±15.12♂	102.51±16.39♂	102.85±16.75♂	102.63±4.51♂	G x T x S	0.93	0.01
	WL	F	82.22±12.34♂	81.88±12.37♂	81.78±12.52♂	81.98±12.63♂	81.97±3.96♂			
		M	96.84±14.56♂	95.75±14.91†♂	96.36±15.86♂	96.17±16.58♂	96.28±4.51♂			
	WL+C	F	78.61±8.97 ♂	78.54±9.03 ♂	78.28±9.01 ♂	78.31±9.14 ♂	78.44±4.12♂			
		M	97.29±20.06♂	96.13±19.26†♂	96.32±19.10♂	96.60±18.93♂	96.59±4.30♂			
Fat Mass (kg)	PLA		29.21±7.98	29.13±8.09	29.26±8.80	29.29±9.19	54.98±1.74	Group	0.67	0.01
	WL		28.01±7.13	27.44±6.92 †	27.38±7.22 †	27.29±7.27	54.91±1.71	Time	0.16	0.03
	WL+C		28.09±7.42	27.85±7.27	27.73±7.38	27.64±6.92	52.59±1.69	G x T	0.56	0.02
	Time		28.43±7.42	28.12±7.36 †	28.11±7.74	28.06±7.77				
	F		30.58±6.58 ♂	30.42±6.57 ♂	30.28±6.84 ♂	30.09±7.11 ♂	30.34±1.21♂	Sex	0.01	0.10
	M		25.86±7.65 ♂	25.38±7.41 †♂	25.51±8.05 ♂	25.64±7.93 ♂	25.58±1.32♂	S x T	0.36	0.02
	PLA	F	31.07±7.57	31.14±7.85	31.24±8.09	31.10±8.91	31.14±2.12	G x S	0.74	0.01
		M	26.98±8.28	26.71±8.09	26.88±9.44	27.12±9.52	26.92±2.32	G x T x S	0.99	0.003
	WL	F	30.92±6.88 ♂	30.44±6.70 ♂	30.29±6.80 ♂	30.06±6.78 ♂	30.43±2.04♂			
		M	24.22±5.75 ♂	23.54±5.24 †♂	23.60±6.13 ♂	23.69±6.51 ♂	23.76±2.32♂			
	WL+C	F	29.71±5.63	29.68±5.43	29.30±5.94	29.10±5.82	29.45±2.12			
		M	26.33±8.93	25.84±8.69	26.01±8.64	26.05±7.93	26.06±2.21			
Fat Free Mass (kg)	PLA		54.02±13.90	53.87±14.04	53.83±14.18	53.70±14.26	29.03±1.57	Group	0.53	0.02
	WL		53.54±12.74	53.52±12.73	53.70±12.97	53.79±12.76	27.10±1.55	Time	0.93	0.002
	WL+C		52.17±14.09	52.09±13.64	52.10±13.59	52.28±13.47	27.75±1.53	G x T	0.90	0.01
	Time		53.23±13.40	53.15±13.29	53.20±13.40	53.25±13.31				
	F		43.48±5.35 ♂	43.50±5.08 ♂	43.49±5.23 ♂	43.57±5.07 ♂	43.46±1.34♂	Sex	<0.001	0.65
	M		64.87±10.47♂	64.67±10.57♂	64.79±10.64♂	64.81±10.55♂	64.86±1.46♂	S x T	0.92	0.002
	PLA	F	42.93±5.33 ♂	42.73±4.65 ♂	42.60±4.82 ♂	42.34±4.42 ♂	42.65±2.34♂	G x S	0.51	0.02
		M	67.33±7.45 ♂	67.25±8.31 ♂	67.31±8.42 ♂	67.33±8.49 ♂	67.30±2.57♂	G x T x S	0.84	0.01
	WL	F	45.01±6.28 ♂	45.05±6.27 ♂	45.14±6.44 ♂	45.42±6.23 ♂	45.15±2.25♂			
		M	64.63±10.10♂	64.53±10.27♂	64.83±10.62♂	64.68±10.65♂	64.67±2.57♂			
	WL+C	F	42.38±4.20 ♂	42.61±3.97 ♂	42.59±4.00 ♂	42.79±4.01 ♂	42.59±2.34♂			
		M	62.85±13.30♂	62.44±12.89♂	62.47±12.73♂	62.63±12.47♂	62.60±2.45♂			
Body Fat (%)	PLA		35.49±8.16	35.44±8.36	35.50±8.66	35.47±8.69	34.86±0.97	Group	0.44	0.03
	WL		34.69±7.64	34.23±7.61	34.06±7.82 †	33.90±7.58 †	33.36±0.95	Time	0.09	0.04
	WL+C		35.38±7.71	35.17±7.62	35.05±7.63	34.93±7.22	34.88±0.95	G x T	0.63	0.02
	Time		35.18±7.72	34.94±7.77	34.86±7.94 †	34.76±7.75 †				
	F		40.98±3.87 ♂	40.79±3.93 ♂	40.65±4.32 ♂	40.40±4.48 †♂	40.73±0.75♂	Sex	<0.001	0.68
	M		28.25±4.92 ♂	27.95±4.85 ♂	27.95±5.25 ♂	28.03±4.89 ♂	28.01±0.82♂	S x T	0.51	0.01
	PLA	F	41.53±4.15 ♂	41.56±4.70 ♂	41.68±4.91 ♂	41.52±5.46 ♂	41.57±1.31♂	G x S	0.74	0.01
		M	28.24±5.23 ♂	28.10±5.13 ♂	28.07±5.76 ♂	28.22±5.70 ♂	28.16±1.44♂	G x T x S	0.95	0.01
	WL	F	40.46±3.70 ♂	40.06±3.73 ♂	39.85±4.02 ♂	39.54±3.82 †♂	39.98±1.26♂			
		M	27.18±3.69 ♂	26.66±3.21 ♂	26.53±4.03 ♂	26.58±3.92 ♂	26.74±1.44♂			
	WL+C	F	41.00±4.03 ♂	40.83±3.45 ♂	40.49±4.19 ♂	40.22±4.19 ♂	40.63±1.31♂			
		M	29.25±5.78 ♂	29.00±5.88 ♂	29.12±5.88 ♂	29.16±5.03 ♂	29.13±1.37♂			

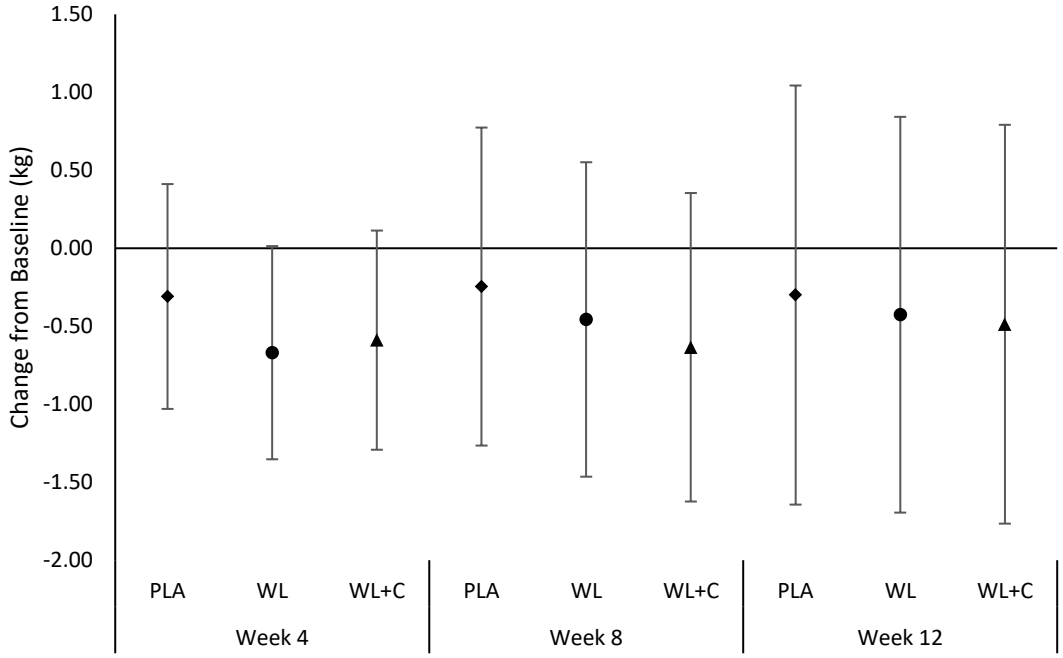

Figure 4. ***Body Weight.*** *Data are presented as Δ-means ± 95% CI. Statistical notation* (§) *denotes a significant difference (p≤0.05) from baseline.*

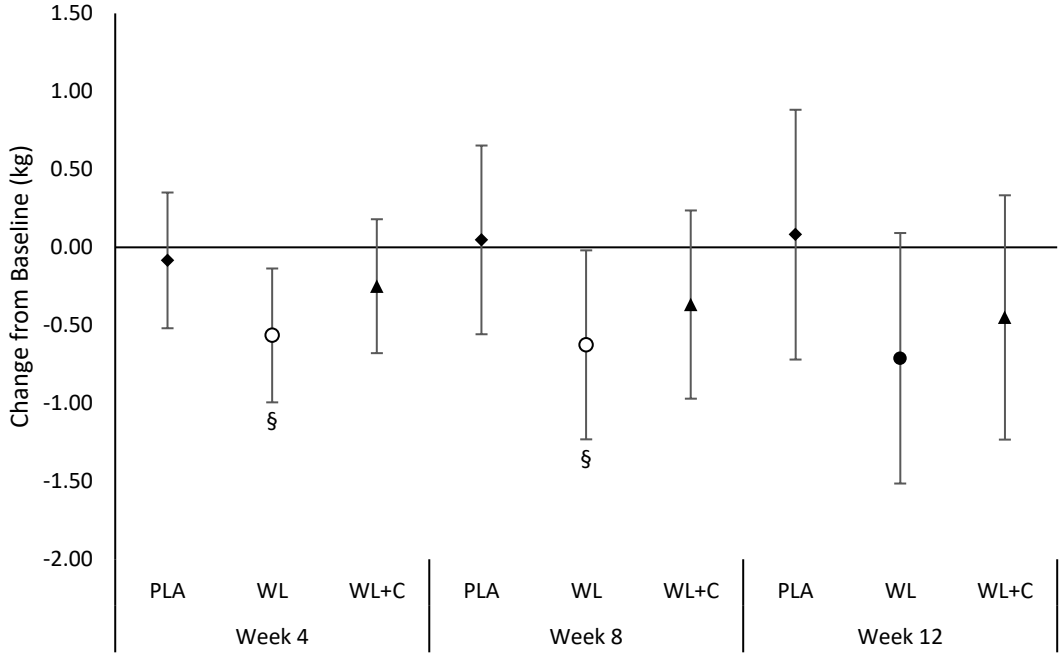

Figure 5. ***Fat Mass.*** *Data are presented as Δ-means ± 95% CI. Statistical notation (§) denotes a significant difference (p≤0.05) from baseline.*

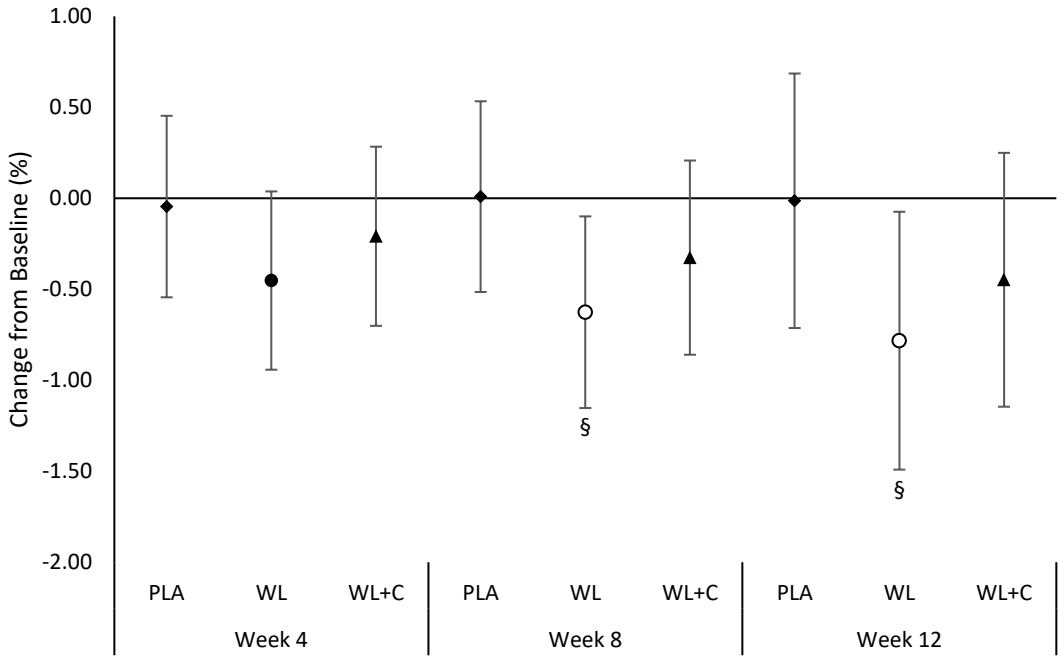

Figure 6. ***Body Fat.*** *Data are presented as Δ-means ± 95% CI. Statistical notation* (§) *denotes a significant difference (p≤0.05) from baseline.*

Anthropometrics. (*Table 7*) Overall Wilks' Lambda Sex ($p<0.01$) effect was observed, with no significant Group ($p=0.81$), Time ($p=0.42$), Group x Time ($p=0.97$), Sex x Time ($p=0.53$), Group x Sex ($p=0.97$), or Group x Time x Sex ($p=0.79$) effects for the anthropometric variables, waist circumference (W/C; cm), hip circumference (H/C; cm), and waist-to-hip (W:H) ratio. Univariate analysis indicated significant effects of sex ($p<0.01$) for W/C and W:H but, no significant group, time, group x time, sex x time, group x sex, or group x time x sex interaction effects for any anthropometric variable. Pairwise analysis showed no real changes within groups other than WL+C increasing W:H, baseline to week 12 (WL+C 0.87±0.07; WL+C 0.89±0.08). Also, general sex differences were observed for W/C (F 94.8±1.56; M 102.12±1.7 cm) and W:H (F 0.84±0.01; M 0.92±0.01) where females had smaller measures than males.

Table 7 – Continued

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Bone Mineral Content (g)	PLA		2.03±0.48	2.00±0.47 †	2.01±0.49	2.01±0.50	2.05±0.08	Group	0.78	0.01
	WL		2.04±0.48	2.04±0.49	2.02±0.46 ‡	2.03±0.48	2.08±0.08	Time	0.17	0.03
	WL+C		1.99±0.60	1.98±0.59	1.99±0.59	1.98±0.59	2.00±0.08	G x T	0.25	0.04
	Time		2.02±0.52	2.01±0.51	2.01±0.51	2.01±0.52				
	F		1.69±0.28 ♂	1.69±0.29 ♂	1.69±0.28 ♂	1.68±0.28 ♂	1.69±0.06 ♂	Sex	<0.001	0.48
	M		2.41±0.46 ♂	2.39±0.46 ♂	2.39±0.46 ♂	2.39±0.47 ♂	2.40±0.07 ♂	S x T	0.26	0.02
	PLA	F	1.65±0.14 ♂	1.65±0.14 ♂	1.64±0.13 ♂	1.64±0.15 ♂	1.64±0.11 ♂	G x S	0.74	0.01
		M	2.48±0.31 ♂	2.43±0.36 †♂	2.46±0.36 ♂‡	2.46±0.37 ♂	2.46±0.12 ♂	G x T x S	0.51	0.03
	WL	F	1.75±0.33 ♂	1.75±0.34 ♂	1.74±0.32 ♂	1.74±0.33 ♂	1.74±0.11 ♂			
		M	2.42±0.37 ♂	2.42±0.38 ♂	2.39±0.35 ♂‡	2.42±0.36 ♂‡	2.41±0.12 ♂			
	WL+C	F	1.68±0.34 ♂	1.68±0.34 ♂	1.68±0.34 ♂	1.67±0.33 ♂	1.67±0.11 ♂			
		M	2.33±0.65 ♂	2.32±0.63 ♂	2.32±0.63 ♂	2.32±0.64 ♂	2.32±0.12 ♂			
Waist Circumference (cm)	PLA		98.00±10.75	98.23±10.14	98.89±10.22	98.89±10.12	98.86±2.03	Group	0.94	0.002
	WL		96.88±9.24	97.74±10.12	97.33±10.85	98.40±9.84	97.88±1.99	Time	0.30	0.02
	WL+C		97.73±10.87	98.72±10.65	98.31±11.13	98.95±11.54	98.64±1.98	G x T	0.98	0.01
	Time		97.53±10.16	98.23±10.16	98.17±10.61	98.74±10.38†				
	F		93.88±9.25 ♂	95.00±9.13 ♂	94.97±9.64 ♂	95.46±9.30 †♂	94.80±1.56 ♂	Sex	0.002	0.14
	M		101.89±9.59 ♂	102.09±10.11♂	101.99±10.59♂	102.67±10.37♂	102.12±1.70 ♂	S x T	0.80	0.005
	PLA	F	94.30±10.92♂	94.26±9.63 ♂	95.46±10.04	95.46±9.68	94.87±2.73 ♂	G x S	0.66	0.01
		M	102.44±9.13 ♂	103.00±8.97 ♂	103.00±9.28	103.00±9.47	102.86±2.99 ♂	G x T x S	0.37	0.03
	WL	F	94.37±9.27	95.31±10.14	96.15±9.98	96.72±9.26 †	95.64±2.63			
		M	100.14±8.57	100.90±9.68	98.87±12.27	100.58±10.62	100.12±2.99			
	WL+C	F	92.92±8.08 ♂	95.40±8.21 †	93.19±9.45 ♂	94.09±9.57 ♂	93.90±2.73 ♂			
		M	102.99±11.41♂	102.35±12.15	103.91±10.41♂	104.26±11.53♂	103.38±2.86 ♂			
Hip Circumference (cm)	PLA		113.09±8.46	114.02±8.13	113.90±9.33	113.15±9.84	113.49±1.70	Group	0.62	0.02
	WL		111.79±7.40	111.40±6.93	111.54±7.04	111.65±7.54	111.45±1.67	Time	0.60	0.01
	WL+C		111.78±8.05	111.65±7.83	111.62±7.84	111.01±7.42	111.51±1.66	G x T	0.68	0.02
	Time		112.21±7.88	112.33±7.62	112.33±8.06	111.92±8.24				
	F		112.96±7.90	112.90±8.04	112.57±8.43	112.58±8.90	112.76±1.31	Sex	0.53	0.01
	M		111.31±7.89	111.66±7.15	112.05±7.72	111.13±7.45 ‡	111.54±1.43	S x T	0.46	0.01
	PLA	F	113.98±10.28	114.47±9.61	114.09±10.62	113.56±11.80	114.03±2.29	G x S	0.91	0.003
		M	112.03±5.95	113.49±6.38	113.67±8.06	112.65±7.45	112.96±2.51	G x T x S	0.87	0.01
	WL	F	113.13±6.12	112.54±7.54	112.05±7.57	112.64±7.99	112.59±2.20			
		M	110.05±8.83	109.92±6.11	110.87±6.61	110.36±7.12	110.30±2.51			
	WL+C	F	111.76±7.41	111.71±7.26	111.60±7.30	111.55±6.93	112.59±2.29			
		M	111.81±9.07	111.59±8.76	111.64±8.75	110.43±8.22	111.37±2.39			
Waist:Hip Ratio	PLA		0.87±0.08	0.86±0.07	0.87±0.06	0.87±0.07	0.87±0.01	Group	0.70	0.01
	WL		0.87±0.06	0.88±0.06	0.87±0.06	0.88±0.06	0.88±0.01	Time	0.17	0.03
	WL+C		0.87±0.07	0.88±0.06	0.88±0.07	0.89±0.08 †	0.88±0.01	G x T	0.90	0.01
	Time		0.87±0.07	0.87±0.06	0.87±0.07	0.88±0.07 †				
	F		0.83±0.05 ♂	0.84±0.05 ♂	0.84±0.05 ♂	0.85±0.06 †♂	0.84±0.01 ♂	Sex	<0.001	0.39
	M		0.92±0.05 ♂	0.91±0.05 ♂	0.91±0.07 ♂	0.92±0.05 ♂	0.92±0.01 ♂	S x T	0.40	0.02
	PLA	F	0.83±0.06 ♂	0.83±0.07 ♂	0.84±0.06 ♂	0.84±0.07 ♂	0.83±0.01 ♂	G x S	0.60	0.02
		M	0.92±0.06 ♂	0.91±0.05 ♂	0.91±0.05 ♂	0.91±0.06 ♂	0.91±0.02 ♂	G x T x S	0.17	0.05
	WL	F	0.83±0.05 ♂	0.85±0.05 ♂	0.86±0.04 ♂	0.86±0.05 †♂	0.85±0.01 ♂			
		M	0.91±0.03 ♂	0.92±0.05 ♂	0.89±0.08 ♂	0.91±0.05 ♂	0.91±0.02 ♂			
	WL+C	F	0.83±0.04 ♂	0.85±0.05 †♂	0.83±0.06 ♂	0.84±0.07 ♂	0.84±0.01 ♂			
		M	0.92±0.06 ♂	0.92±0.07 ♂	0.93±0.06 ♂	0.94±0.05 ♂	0.93±0.01 ♂			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.94), Time (p=0.07), Group x Time (p=0.88), Sex (p<0.01), Sex x Time (p=0.67), and Group x Sex (p=0.94), Group x Time x Sex (p=0.99) effects for body composition variables; and an overall Wilks' Lambda Group (p=0.81), Time (p=0.42), Group x Time (p=0.97), Sex (p<0.01), Sex x Time (p=0.53), and Group x Sex (p=0.97), Group x Time x Sex (p=0.79) effects for anthropometric variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Resting Energy Expenditure

Energy Expenditure. Overall Wilks' Lambda Time ($p<0.01$), Sex ($p<0.01$), and Group x Time ($p<0.05$), effects were revealed, with no observed Group ($p=0.70$), Sex x Time ($p=0.80$), Group x Sex ($p=0.75$), or Group x Time x Sex ($p=0.16$) effects for resting energy expenditure (REE; kcal/d) and resting energy expenditure per kilogram (REE/kg; kcal/kg/d). Univariate analysis indicated time ($p<0.01$), sex ($p<0.01$), and group x time ($p<0.05$) effects, with no significant group, sex x time, group x sex, or group x time x sex interaction effects for resting energy expenditure measures.

Pairwise analysis showed an increased REE for all groups, throughout the study. PLA raised baseline to weeks 4 and 8 (PLA 1,549.05±382.89; Wk4 1,711.22±375.83; Wk8 1,683.77±413.7 kcal/d) as WL increased from week 8 to 12 (WL 1,625.98±372.23; WL 1,725.34±418.95 kcal/d) and WL+C increased from baseline to week 12 (WL+C 1,570.94±407.92; WL+C 1,681.45±317.91 kcal/d). A majority of WL+C changed between weeks 8 and 12 (WL+C 1,589.33±289.56; WL+C 1,681.45±317.91 kcal/d). Assessment of REE per kilogram was similar to unweighted REE. Baseline, REE/kg was lower in PLA than WL (PLA 17.23±3.08; WL 18.95±2.14 kcal/kg/d) and PLA increased from baseline at weeks 4 and 8 (PLA 17.23±3.08; Wk4 19.06±2.72; Wk8 18.61±2.36 kcal/kg/d). Whereas, WL saw increase between weeks 8 and 12 (WL 18.45±2.69; WL 19.57±3.23 kcal/kg/d), and WL+C increased from baseline at weeks 4 and 12 (WL+C 17.84±1.98; Wk4 18.84±1.83; Wk12 19.41±1.93 kcal/kg/d). Analysis of change from baseline [95% CI] (*Figures 7-9*) also indicated increases at weeks 4, 8, and 12 in REE (PLA 162±277 [68, 266]; PLA 135±310 [31, 248]; WL+C 111±220 [10, 207] kcal/d) and

REE/kg (PLA 1.84±2.65 [0.84, 2.88]; PLA 1.38±2.75 [0.34, 2.49]; WL+C 1.57±2.37 [0.5, 2.6] kcal/kg/d). Overall sex differences were seen for REE (F 1,429.42±39.06; M 1,898.96±42.68 kcal/d) and REE/kg (F 17.96±0.32; M 19.41±0.34 kcal/kg/d), with males expending more kcals and kcals/kg. *Table 8* presents the REE data within each group. These data fail to reject $H_0$4: Resting energy expenditure will improve significantly in treatment groups compared to baseline and/or placebo.

Table 8: Resting Energy Expenditure Data

			Weeks				Mean			
	Group		**0**	**4**	**8**	**12**	**(SEM)**	**Effect**	**p-Level**	η_p^2
Resting Energy Expenditure (kcal/d)	PLA		1,549±383	1,711±376 †	1,684±414 †	1,641±393	1,672±51	Group	0.63	0.01
	WL		1,670±304	1,642±300	1,626±372	1,725±419 ‡	1,694±50	Time	0.01	0.07
	WL+C		1,571±408	1,629±304	1,589±290	1,681±318 †‡	1,627±50	G x T	0.02	0.08
	Time		1,597±366	1,660±325 †	1,632±358	1,683±375 †‡				
	F		1,394±210 ♂	1,457±179 ♂	1,422±227 ♂	1,450±219 ♂	1,429±39 ♂	Sex	<0.001	0.52
	M		1,840±366 ♂	1,903±292 ♂	1,883±324 ♂	1,961±331 †‡♂	1,899±43 ♂	S x T	0.52	0.01
	PLA	F	1,323±206 ♂	1,439±174 ♂	1,408±227 ♂	1,370±231 ♂	1,385±69 ♂	G x S	0.44	0.03
		M	1,821±374 ♂	2,038±273 †♂	2,015±336 c†♂	1,966±283 ♂	1,960±75 ♂	G x T x S	0.12	0.05
	WL	F	1,520±147 ♂	1,491±206 ♂	1,425±229 ♂	1,492±209 ♂	1,482±66 ♂			
		M	1,865±350 ♂	1,839±295 ♂	1,888±367 ♂	2,029±435 †‡♂	1,905±75 ♂			
	WL+C	F	1,329±223 ♂	1,438±161 ♂	1,434±245 ♂	1,486±214 †♂	1,422±69 ♂			
		M	1,835±406 ♂	1,838±289 ♂	1,759±240 a♂	1,895±276 ♂‡	1,832±72 ♂			
Resting Energy Expenditure (kcal/kg/d)	PLA		17.23±3.08 b	19.06±2.72 †	18.61±2.36 †	18.26±2.79	18.37±0.41	Group	0.50	0.02
	WL		18.95±2.14 a	18.79±2.34	18.45±2.69	19.57±3.23 ‡	19.04±0.40	Time	<0.001	0.09
	WL+C		17.84±1.98	18.84±1.83 †	18.43±2.19	19.41±1.93 †‡	18.65±0.40	G x T	0.03	0.07
	Time		18.02±2.51	18.90±2.29 †	18.49±2.39	19.09±2.73 †‡				
	F		17.45±2.33 ♂	18.31±2.18 †♂	17.85±2.32 ♂	18.27±2.54 †♂	17.96±0.32♂	Sex	0.003	0.13
	M		18.69±2.59 ♂	19.59±2.26 †♂	19.27±2.27 ♂	20.07±2.66 †‡♂	19.41±0.34♂	S x T	0.74	0.01
	PLA	F	16.64±2.26 b	18.21±2.70 †	17.67±2.05 ♂	17.43±3.03	17.49±0.55♂	G x S	0.77	0.01
		M	17.93±3.87	20.09±2.50 †	19.73±2.31 †♂	19.26±2.23	19.25±0.61♂	G x T x S	0.12	0.05
	WL	F	18.75±2.49 ac	18.34±2.09	17.54±2.40 ♂	18.35±2.24 ♂	18.24±0.53♂			
		M	19.21±1.68	19.37±2.62	19.64±2.69 ♂	21.16±3.73 †‡♂	19.84±0.61♂			
	WL+C	F	16.86±1.67 b♂	18.39±1.85 †	18.35±2.59 †	19.03±2.24 †	18.16±0.55			
		M	18.90±1.78 ♂	19.34±1.77	18.51±1.77	19.83±1.51 *	19.15±0.58			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.70), Time (p<0.01), Group x Time (p<0.05), Sex (p<0.01), Sex x Time (p=0.80), and Group x Sex (p=0.75), Group x Time x Sex (p=0.16) effects for resting energy expenditure values. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

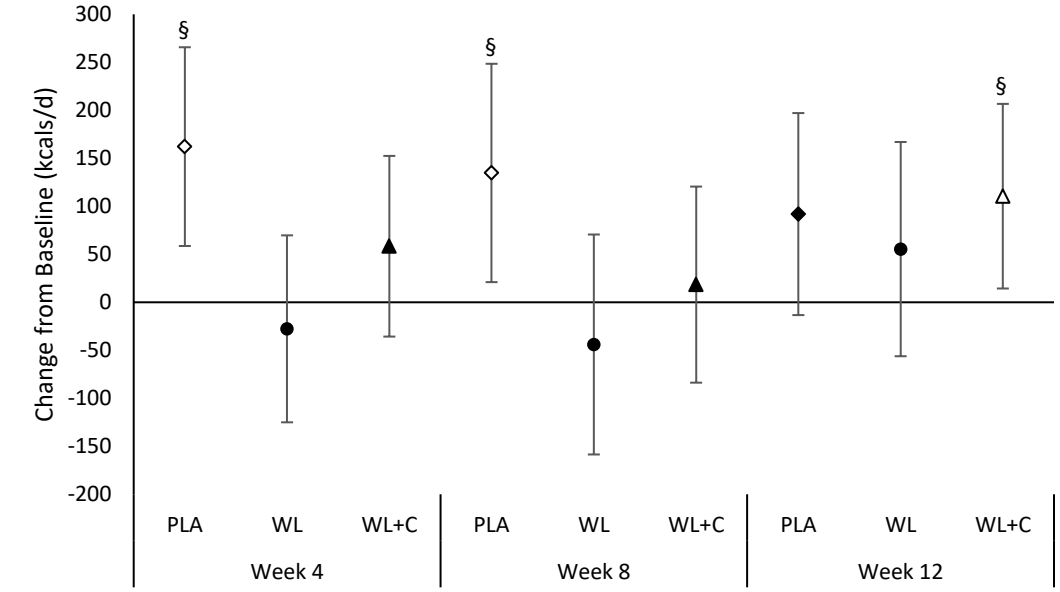

Figure 7. ***Resting Energy Expenditure.*** *Data are presented as Δ-means ± 95% CI. Statistical notation* (§) *denotes a significant difference (p≤0.05) from baseline.*

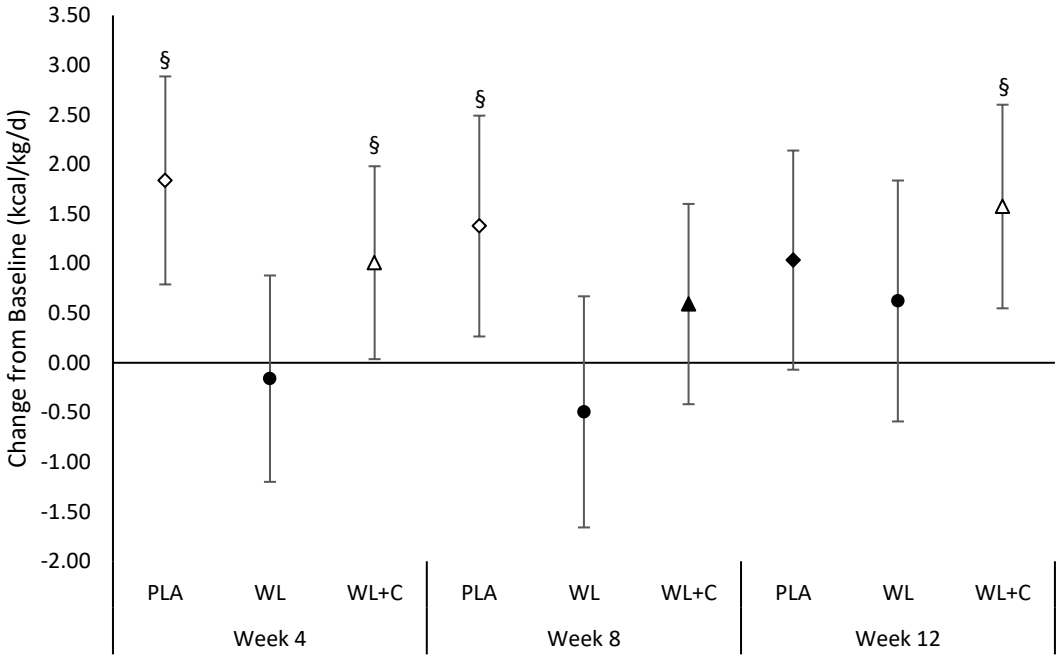

Figure 8. ***Resting Energy Expenditure per Kilogram.*** *Data are presented as Δ-means ± 95% CI. Statistical notation* (§) *denotes a significant difference (p≤0.05) from baseline.*

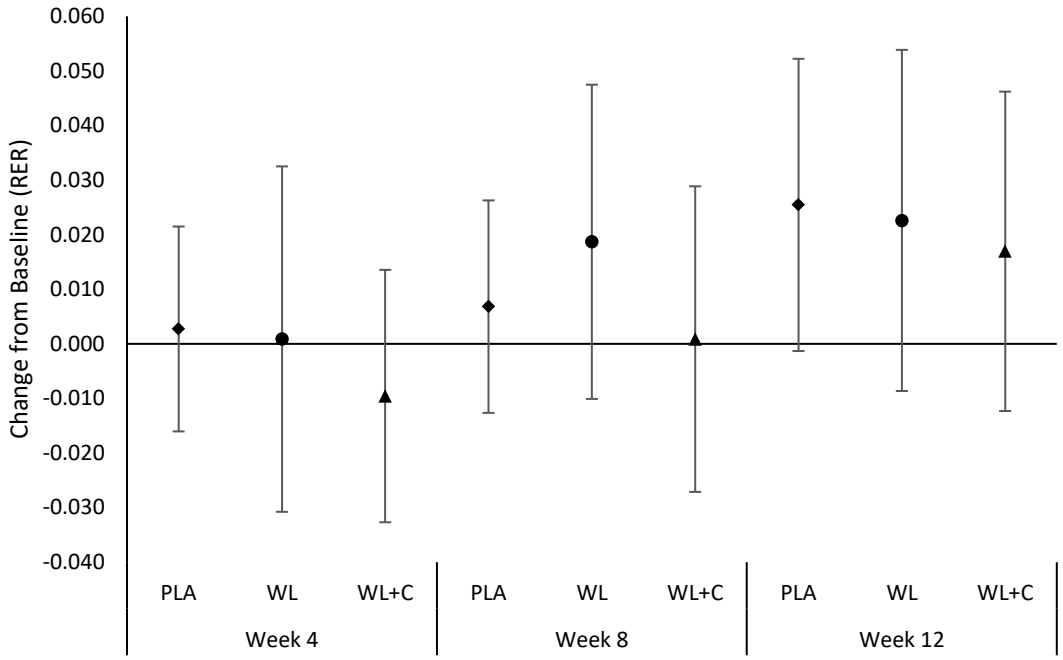

Figure 9. ***Respiratory Exchange Ratio.*** *Data are presented as Δ-means ± 95% CI. Statistical notation* (§) *denotes a significant difference (p≤0.05) from baseline.*

Total Body Water. Overall Wilks' Lambda Sex ($p<0.01$) effect was observed, with no significant Group ($p=0.70$), Time ($p=0.42$), Group x Time ($p=0.34$), Sex x Time ($p=0.29$), Group x Sex ($p=0.43$), or Group x Time x Sex ($p=0.75$) effects for body water variables total body water (TBW; L; %), intracellular water (ICW; L; %), or extracellular water (ECW; L; %). Univariate analysis also indicated significant effects of sex ($p<0.001$) with no group, time, group x time, sex x time, group x sex, or group x time x sex interaction effects for body water variable. Pairwise analysis showed WL+C decrease from baseline at weeks 4, 8, and 12 in TBW (WL+C 38.8±9.6; Wk4 37.5±8.3; Wk8 36.8±8.4; Wk12 37.2±8.2 L) and ICW (WL+C 22.6±5.5; Wk4 21.6±4.5; Wk8 21.2±4.7; Wk12 21.6±4.5 L). Baseline ECW reduced at weeks 8 and 12 (WL+C 16.2±4.4; Wk8 15.7±3.7; Wk12 15.7±3.7 L). Generally, males had larger body water measures, i.e. TBW (F 32.4±0.9; M

45.1±1.0 L), ICW (F 19.1±0.5; M 25.7±0.6 L), ECW (F 13.3±0.4; M 19.4±0.4 L), TBW% (F 40.6±0.5; M 45.6±0.6%), and ECW% (F 41.1±0.2; M 43.1±0.2%); besides ICW% (F 58.9±0.2; M 56.9±0.2%). Lastly, groups differed by sex at all time points, except PLA ICW% and ECW% at week 8 (ICW F 58.0±2.6; M 56.9±1.7 | ECW F 42.0±2.6; M 43.1±1.7%) and week 12 (ICW F 58.5±1.8; M 57.3±3.6 | ECW F 41.5±1.8; M 42.7±3.6%). *Table 9* presents the body water data.

Table 9: Total Body Water Data

			Weeks				Mean			
Variable	**Group**		**0**	**4**	**8**	**12**	**SEM**		**p-Level**	**η_p^2**
Total Body Water (L)	PLA		39.4 ± 9.6	39.0 ± 9.1	38.5 ± 9.4	39.8 ± 9.8[‡]	39.9 ± 1.1	Group	0.45	0.03
	WL		37.6 ± 7.1	37.8 ± 7.5	38.2 ± 7.3	38.0 ± 7.7	38.6 ± 1.1	Time	0.12	0.03
	WL+C		38.8 ± 9.6	37.5 ± 8.3[†]	36.8 ± 8.4[†]	37.2 ± 8.2[†]	37.9 ± 1.1	G x T	0.06	0.07
	Time		38.6 ± 8.7	38.1 ± 8.2[†]	37.8 ± 8.3[†]	38.3 ± 8.5				
	F		32.5 ± 4.2[♂]	32.5 ± 4.6[♂]	32.2 ± 4.3[♂]	32.7 ± 4.5[♂]	32.4 ± 0.9[♂]	Sex	<0.001	0.61
	M		46.0 ± 6.7[♂]	44.7 ± 6.5[†♂]	44.6 ± 6.7[†♂]	45.1 ± 7.2[♂]	45.1 ± 1.0[♂]	S x T	0.26	0.02
	PLA	F	32.1 ± 4.6[♂]	32.3 ± 4.8[♂]	31.3 ± 4.4[♂]	32.9 ± 5.4[♂‡]	32.2 ± 1.5[♂]	G x S	0.22	0.05
		M	48.1 ± 6.0[♂]	47.0 ± 5.9[♂]	47.1 ± 5.6[♂]	48.1 ± 7.1[♂]	47.6 ± 1.7[♂]	G x T x S	0.63	0.02
	WL	F	33.3 ± 4.5[♂]	33.7 ± 5.4[♂]	34.1 ± 5.0[♂]	33.5 ± 4.9[♂]	33.6 ± 1.5[♂]			
		M	43.3 ± 5.6[♂]	43.1 ± 6.6[♂]	43.5 ± 6.5[♂]	44.0 ± 6.6[♂]	43.5 ± 1.7[♂]			
	WL+C	F	31.9 ± 3.8[♂]	31.5 ± 3.3[♂]	31.0 ± 2.8[♂]	31.5 ± 2.8[♂]	31.5 ± 1.5[♂]			
		M	46.4 ± 8.0[♂]	44.0 ± 6.9[†♂]	43.3 ± 7.6[†♂]	43.4 ± 7.5[†♂]	44.3 ± 1.6[♂]			
Intracellular Water (L)	PLA		22.7 ± 5.2	22.5 ± 4.9	22.1 ± 5.2	23.0 ± 6.0[‡]	23.0 ± 0.7	Group	0.55	0.02
	WL		21.7 ± 4.1	22.2 ± 4.5	22.2 ± 4.4	22.1 ± 4.4	22.4 ± 0.7	Time	0.23	0.02
	WL+C		22.6 ± 5.5	21.6 ± 4.5[†]	21.2 ± 4.7[†]	21.6 ± 4.5[†]	21.9 ± 0.7	G x T	0.07	0.06
	Time		22.3 ± 4.9	22.1 ± 4.6	21.8 ± 4.7[†]	22.2 ± 5.0				
	F		19.1 ± 2.9[♂]	19.3 ± 3.1[♂]	18.9 ± 2.9[♂]	19.2 ± 2.7[♂]	19.1 ± 0.5[♂]	Sex	<0.001	0.52
	M		26.1 ± 4.1[♂]	25.4 ± 3.8[♂]	25.3 ± 4.0[†♂]	25.8 ± 4.7[♂]	25.7 ± 0.6[♂]	S x T	0.45	0.01
	PLA	F	18.8 ± 2.8[♂]	19.0 ± 2.8[♂]	18.2 ± 2.9[♂]	19.2 ± 3.1[♂]	18.8 ± 0.9[♂]	G x S	0.21	0.05
		M	27.3 ± 3.4[♂]	26.7 ± 3.2[♂]	26.8 ± 3.0[♂]	27.6 ± 5.4[♂]	27.1 ± 1.0[♂]	G x T x S	0.81	0.01
	WL	F	19.5 ± 2.9[♂]	20.3 ± 3.9[♂]	20.2 ± 3.4[♂]	19.8 ± 3.2[♂]	20.0 ± 0.9[♂]			
		M	24.6 ± 3.7[♂]	24.6 ± 4.2[♂]	24.8 ± 4.3[♂]	25.1 ± 4.1[♂]	24.8 ± 1.0[♂]			
	WL+C	F	19.0 ± 3.2[♂]	18.5 ± 2.1[♂]	18.1 ± 1.8[♂]	18.6 ± 1.8[♂]	18.6 ± 0.9[♂]			
		M	26.5 ± 4.9[♂]	25.0 ± 4.1[†♂]	24.5 ± 4.6[†♂]	24.7 ± 4.5[†♂]	25.2 ± 1.0[♂]			
Extracellular Water (L)	PLA		16.7 ± 4.4	16.5 ± 4.2	16.4 ± 4.3	16.7 ± 4.3	16.9 ± 0.5	Group	0.32	0.04
	WL		15.9 ± 3.1	15.6 ± 3.4	16.0 ± 3.2	15.9 ± 3.4	16.2 ± 0.5	Time	0.13	0.03
	WL+C		16.2 ± 4.4	15.9 ± 3.8	15.7 ± 3.7[†]	15.7 ± 3.7[†]	16.0 ± 0.4	G x T	0.32	0.04
	Time		16.3 ± 4.0	16.0 ± 3.8[†]	16.0 ± 3.7[†]	16.1 ± 3.8				
	F		13.3 ± 1.5[♂]	13.2 ± 1.8[♂]	13.3 ± 1.6[♂]	13.4 ± 1.9[♂]	13.3 ± 0.4[♂]	Sex	<0.001	0.69
	M		19.8 ± 2.9[♂]	19.3 ± 2.7[†♂]	19.3 ± 2.8[†♂]	19.3 ± 2.8[†♂]	19.4 ± 0.4[♂]	S x T	0.18	0.03
	PLA	F	13.3 ± 1.8[♂]	13.3 ± 2.0[♂]	13.1 ± 1.7[♂]	13.7 ± 2.5[♂]	13.4 ± 0.6[♂]	G x S	0.28	0.04
		M	20.8 ± 2.8[b♂]	20.3 ± 2.8[♂]	20.3 ± 2.9[♂]	20.4 ± 2.7[♂]	20.5 ± 0.7[♂]	G x T x S	0.49	0.03
	WL	F	13.7 ± 1.6[♂]	13.4 ± 2.1[♂]	13.8 ± 1.7[♂]	13.7 ± 1.8[♂]	13.7 ± 0.6[♂]			
		M	18.7 ± 2.0[a♂]	18.5 ± 2.4[♂]	18.8 ± 2.3[♂]	18.9 ± 2.6[♂]	18.7 ± 0.7[♂]			
	WL+C	F	12.9 ± 1.0[♂]	13.0 ± 1.4[♂]	12.9 ± 1.0[♂]	12.9 ± 1.2[♂]	12.9 ± 0.6[♂]			
		M	19.9 ± 3.4[♂]	19.0 ± 2.9[†♂]	18.7 ± 3.1[†♂]	18.7 ± 3.1[†♂]	19.1 ± 0.6[♂]			

Table 9 – Continued

Variable	Group		Weeks 0	4	8	12	Mean SEM		p-Level	η_p^2
Total Body Water (%)	PLA		43.2 ± 4.2	43.0 ± 4.3	42.6 ± 4.9	43.3 ± 6.4	43.3 ± 0.7	Group	0.58	0.02
	WL		42.9 ± 3.3	42.9 ± 3.8	43.4 ± 3.5	43.2 ± 3.9	43.3 ± 0.6	Time	0.65	0.01
	WL+C		42.5 ± 5.6	42.2 ± 3.6	42.2 ± 4.5	42.7 ± 3.6	42.5 ± 0.6	G x T	0.89	0.01
	Time		42.9 ± 4.4	42.7 ± 3.9	42.7 ± 4.3	43.1 ± 4.7				
	F		40.8 ± 3.2♂	40.7 ± 3.2♂	40.3 ± 3.6♂	40.5 ± 3.5♂	40.6 ± 0.5♂	Sex	<0.001	0.42
	M		45.4 ± 4.4♂	45.1 ± 3.1♂	45.6 ± 3.2♂	46.1 ± 4.2♂	45.6 ± 0.6♂	S x T	0.38	0.02
	PLA	F	40.3 ± 2.7♂	40.4 ± 2.9♂	39.5 ± 3.6♂	40.0 ± 4.1♂	40.1 ± 0.9♂	G x S	0.33	0.04
		M	46.8 ± 2.6♂	46.2 ± 3.6♂	46.3 ± 3.6♂	47.2 ± 6.7♂	46.6 ± 1.0♂	G x T x S	0.85	0.01
	WL	F	41.4 ± 3.2♂	41.3 ± 4.0♂	41.9 ± 3.3♂	41.1 ± 3.6♂	41.4 ± 0.9♂			
		M	44.8 ± 2.3♂	45.0 ± 2.2♂	45.4 ± 2.8♂	45.9 ± 2.2♂	45.3 ± 1.0♂			
	WL+C	F	40.7 ± 3.8♂	40.2 ± 2.6♂	39.5 ± 3.7♂	40.4 ± 2.9♂	40.2 ± 0.9♂			
		M	44.5 ± 6.6♂	44.3 ± 3.4♂	45.2 ± 3.4♂	45.2 ± 2.6♂	44.8 ± 0.9♂			
Intracellular Water (%)	PLA		57.7 ± 1.4	57.9 ± 1.4	57.5 ± 2.3	57.9 ± 2.8	57.7 ± 0.3	Group	0.69	0.01
	WL		57.8 ± 1.7	58.7 ± 3.1	58.2 ± 2.2	58.2 ± 1.5	58.0 ± 0.3	Time	0.49	0.01
	WL+C		58.2 ± 2.9	57.8 ± 1.7	57.5 ± 1.6	58.1 ± 1.8	57.9 ± 0.3	G x T	0.54	0.03
	Time		57.9 ± 2.1	58.1 ± 2.2	57.8 ± 2.0	58.0 ± 2.1				
	F		58.8 ± 1.9♂	59.2 ± 2.3♂	58.6 ± 2.1♂‡	58.9 ± 1.5♂	58.9 ± 0.2♂	Sex	<0.001	0.38
	M		56.8 ± 1.8♂	56.8 ± 1.2♂	56.8 ± 1.5♂	57.0 ± 2.2♂	56.9 ± 0.2♂	S x T	0.64	0.01
	PLA	F	58.5 ± 1.0♂	58.8 ± 0.7♂	58.0 ± 2.6	58.5 ± 1.8	58.4 ± 0.4♂	G x S	0.51	0.02
		M	56.7 ± 1.3♂	56.8 ± 1.1♂	56.9 ± 1.7	57.3 ± 3.6	56.9 ± 0.4♂	G x T x S	0.88	0.01
	WL	F	58.6 ± 1.2♂	60.0 ± 3.5†♂	59.3 ± 1.9♂	59.0 ± 1.2♂	59.2 ± 0.4♂			
		M	56.6 ± 1.7♂	57.0 ± 1.3♂	56.8 ± 1.7♂	57.0 ± 1.1♂	56.8 ± 0.4♂			
	WL+C	F	59.4 ± 2.9♂	58.8 ± 1.2♂	58.4 ± 1.5♂	59.2 ± 1.4♂	59.2 ± 0.4♂			
		M	56.9 ± 2.4♂	56.7 ± 1.4♂	56.6 ± 1.3♂	56.8 ± 1.3♂	56.8 ± 0.4♂			
Extracellular Water (%)	PLA		42.3 ± 1.4	42.1 ± 1.3	42.5 ± 2.3	42.1 ± 2.8	42.3 ± 0.3	Group	0.68	0.01
	WL		42.2 ± 1.7	41.3 ± 3.1	41.8 ± 2.2	41.8 ± 1.5	42.0 ± 0.3	Time	0.50	0.01
	WL+C		41.8 ± 2.9	42.2 ± 1.7	42.5 ± 1.6	42.0 ± 1.8	42.1 ± 0.3	G x T	0.54	0.03
	Time		42.1 ± 2.1	41.9 ± 2.2	42.2 ± 2.0	42.0 ± 2.1				
	F		41.2 ± 1.9♂	40.8 ± 2.3♂	41.4 ± 2.1♂‡	41.1 ± 1.5♂	41.1 ± 0.2♂	Sex	<0.001	0.38
	M		43.2 ± 1.8♂	43.2 ± 1.2♂	43.2 ± 1.5♂	43.0 ± 2.2♂	43.1 ± 0.2♂	S x T	0.66	0.01
	PLA	F	41.5 ± 1.0♂	41.3 ± 0.7♂	42.0 ± 2.6	41.5 ± 1.8	41.6 ± 0.4♂	G x S	0.50	0.02
		M	43.3 ± 1.3♂	43.2 ± 1.1♂	43.1 ± 1.7	42.7 ± 3.6	43.1 ± 0.4♂	G x T x S	0.88	0.01
	WL	F	41.4 ± 1.2♂	40.0 ± 3.5†♂	40.7 ± 1.9♂	41.0 ± 1.2♂	40.8 ± 0.4♂			
		M	43.4 ± 1.7♂	43.0 ± 1.3♂	43.3 ± 1.7♂	43.0 ± 1.1♂	43.2 ± 0.4♂			
	WL+C	F	40.6 ± 2.9♂	41.2 ± 1.2♂	41.6 ± 1.5♂	40.8 ± 1.4♂	41.1 ± 0.4♂			
		M	43.1 ± 2.4♂	43.3 ± 1.4♂	43.4 ± 1.3♂	43.2 ± 1.3♂	43.2 ± 0.4♂			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.70), Time (p=0.42), Group x Time (p=0.34), Sex (p<0.01), Sex x Time (p=0.29), and Group x Sex (p=0.43), Group x Time x Sex (p=0.75) effects for body water variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Biochemical Markers

Blood Glucose and Lipid Profiles

Blood Glucose. Overall Wilks' Lambda showed no significant Time ($p=0.78$), Group x Time ($p=0.67$), Sex x Time ($p=0.34$), or Group x Time x Sex ($p=0.45$) effects on glucose (mmol/L). Univariate analysis found no significant time, group x time, sex, sex x time, or group x time x sex interaction effects for glucose as well. In following, pairwise analysis indicated no real effects on blood glucose from any of the treatment groups.

Lipid Profile. Overall Wilks' Lambda revealed effects of Time ($p<0.05$) and Sex ($p<0.01$), with no Group ($p=0.93$), Group x Time ($p=0.21$), Sex x Time ($p=0.14$), Group x Sex ($p=0.98$), or Group x Time x Sex ($p=0.26$) effects for lipid variables, triglycerides (mmol/L), total cholesterol (Chol; mmol/L), low or high density lipoprotein (LDL; U/L | HDL; mmol/L). Univariate analysis had significant sex ($p<0.001$) effects for HDL and triglycerides as well as time ($p<0.01$) and group x time ($p<0.05$) interaction effects for HDL but, were not present in other lipid measures. No significant group, sex x time, group x sex, or group x time x sex interactions were observed for any lipid measure.

Pairwise analysis exhibited no significant differences in triglycerides, total cholesterol, or LDL. However, supplement groups both presented significant baseline changes in HDL at weeks 8 and 12 wherein, WL increased (WL 1.23±0.39; Wk8 1.31±0.36; Wk12 1.35±0.38 mmol/L) and WL+C decreased (WL+C 1.18±0.36; Wk8 1.31±0.38; Wk12 1.28±0.35 mmol/L). Moreover, males overall had greater triglyceride (F 1.00±0.15; M 1.82±0.17 mmol/L) and lesser HDL (F 1.47±0.06; M 1.09±0.06 mmol/L) levels than females.

Hormones. Overall Wilks' Lambda indicated a significant effect of Sex ($p<0.01$) but, no Group ($p=0.53$), Time ($p=0.15$), Group x Time ($p=0.83$), Sex x Time ($p=0.48$), Group x Sex ($p=0.87$), or Group x Time x Sex ($p=0.15$) effects for hormone variables, insulin (µU/mL), homeostatic model of insulin resistance (HOMA-IR), or leptin (ng/mL). Univariate analysis showed significant sex ($p<0.001$) interaction effects for leptin only, with no group, time, group x time, sex x time, group x sex, or group x time x sex effects for any of the hormone variables.

Pairwise analysis showed WL+C as greater than WL at baseline for insulin (WL+C 15.84±7.32; WL 10.83±7.23 µU/mL) and HOMA-IR (WL+C 3.65±1.81; WL 2.43±1.88 µU/mL). The differences were primarily between males for both insulin (WL+C 18.37±7.58; WL 9.66±9.57 µU/mL) and HOMA-IR (WL+C 4.32±1.92; WL 2.23±2.48 µU/mL). Subsequently, only males of WL increased from baseline to week 12, albeit in just insulin (WL 9.66±9.57; WL 15.88±15.19 µU/mL). Sex differences were present for Leptin at all time points, where females, overall, had greater levels than males (F 55.44±3.51; M 21.42±3.84 ng/mL), in each group. Otherwise, no other differences were observed. *Table 10* presents glucose and lipid related data in each group.

Serum and Whole Blood Clinical Markers

Serum. An Overall Wilks' Lambda revealed Time ($p<0.01$), Sex ($p<0.01$), and Sex x Time ($p=0.06$), with no Group ($p=0.52$), Group x Time ($p=0.24$), Group x Sex ($p=0.57$), or Group x Time x Sex ($p=0.43$) effects for liver function related variables, creatine kinase (CK; U/L), lactate dehydrogenase (LDH; U/L), alanine aminotransferase [transaminase] (ALT; U/L), blood urea nitrogen (BUN; mmol/L), creatinine (Cr; µmol/L), or blood urea

nitrogen to creatinine ratio (BUN:Cr). Univariate analysis indicated effects of group ($p \leq 0.05$) for BUN:Cr, sex ($p < 0.001$) for CK, ALT, BUN, Cr, and LDH ($p < 0.05$) as well as time ($p < 0.001$) for BUN, Cr, and BUN:Cr with no group x time, sex x time, or group x time x sex effects among any of the liver function related variables. Other clinical markers measured but excluded from the previous analysis are aspartate aminotransferase (AST; U/L) and alkaline phosphatase (ALP; U/L).

Pairwise analysis indicated some variation in serum markers, all of which stayed within normal ranges. This is further evidenced by an assessment of change from baseline to week 12 (*Table 12*), showing no change in kidney, muscle, or liver markers for ≥78% of the participants in any given group; with the other ≤22% comprised of those whom increased from normal to high (≤13%) or decreased high to normal (≤13%). Chi-squared analysis showed no significant change in any serum marker among treatments. Nevertheless, males had generally greater values than females for CK (F 95.36±11.39; M 168.43±12.45 U/L), LDH (F 143.07±3.36; M 153.23±3.67 U/L), ALT (F 20.18±2.45; M 33.80±2.68 U/L), BUN (F 3.05±0.12; M 3.64±0.13 mmol/L), and Cr (F 70.92±2.10; M 88.50±2.30 µmol/L). *Table 11* presents the serum chemistry results within each group. *Table 12* shows chi-squared analysis of changes from baseline values observed; Note: ALP has an N of 58 (PLA 18; WL 21; WL+C 19) due to the discontinuation of the reagent near the end of data collection.

Table 10: Glucose and Lipid Responses

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Glucose	PLA		5.05 ± 0.47	5.15 ± 0.53	4.95 ± 0.31 ‡	4.99 ± 0.47	5.04 ± 0.09	Group	0.27	0.04
(mmol/L)	WL		4.90 ± 0.54	4.91 ± 0.52	4.91 ± 0.42 c	4.99 ± 0.63	4.94 ± 0.09	Time	0.77	0.01
	WL+C		5.14 ± 0.60	5.12 ± 0.71	5.15 ± 0.45 b	5.11 ± 0.46	5.14 ± 0.09	G x T	0.63	0.02
	Time		5.03 ± 0.54	5.06 ± 0.59	5.00 ± 0.41	5.03 ± 0.52				
	F		4.96 ± 0.52	4.92 ± 0.60 ♂	4.97 ± 0.38	4.93 ± 0.62	4.95 ± 0.07	Sex	0.08	0.05
	M		5.12 ± 0.55	5.22 ± 0.55 ♂	5.05 ± 0.44	5.14 ± 0.36	5.13 ± 0.07	S x T	0.37	0.02
	PLA	F	5.05 ± 0.43	5.15 ± 0.47	5.03 ± 0.31	4.88 ± 0.49	5.03 ± 0.12	G x S	0.40	0.03
		M	5.05 ± 0.54	5.16 ± 0.62	4.85 ± 0.30 c‡	5.12 ± 0.43 ‡	5.05 ± 0.13	G x T x S	0.59	0.02
	WL	F	4.84 ± 0.57	4.79 ± 0.63	4.83 ± 0.44	4.95 ± 0.81	4.86 ± 0.11			
		M	4.98 ± 0.51	5.06 ± 0.29	5.01 ± 0.40	5.03 ± 0.27	5.02 ± 0.13			
	WL+C	F	4.98 ± 0.57	4.84 ± 0.67 ♂	5.05 ± 0.37	4.97 ± 0.52	4.86 ± 0.12 ♂			
		M	5.31 ± 0.60	5.41 ± 0.65 ♂	5.27 ± 0.52 a	5.27 ± 0.35 ‡	5.31 ± 0.12 ♂			
Insulin	PLA		13.06 ± 8.56	-	-	14.56 ± 10.15	13.96 ± 1.73	Group	0.25	0.04
(µU/mL)	WL		10.83 ± 7.23 c	-	-	13.64 ± 11.87	12.30 ± 1.70	Time	0.07	0.05
	WL+C		15.84 ± 7.32 b	-	-	16.62 ± 8.48	16.30 ± 1.69	G x T	0.60	0.02
	Time		13.24 ± 7.88	-	-	14.95 ± 10.18				
	F		12.49 ± 6.17	-	-	13.29 ± 7.43	12.92 ± 1.33	Sex	0.20	0.03
	M		14.14 ± 9.56	-	-	16.92 ± 12.57	15.45 ± 1.46	S x T	0.31	0.02
	PLA	F	12.29 ± 7.23	-	-	12.22 ± 6.93	12.26 ± 2.34	G x S	0.85	0.01
		M	13.97 ± 10.26	-	-	17.37 ± 12.87	15.67 ± 2.56	G x T x S	0.16	0.06
	WL	F	11.73 ± 5.03	-	-	11.92 ± 8.83	11.82 ± 2.25			
		M	9.66 ± 9.57 c	-	-	15.88 ± 15.19 †	12.77 ± 2.56			
	WL+C	F	13.52 ± 6.54	-	-	15.85 ± 6.07	14.69 ± 2.34			
		M	18.37 ± 7.58 b	-	-	17.45 ± 10.77	17.91 ± 2.44			
Insulin Sensitivity	PLA		2.92 ± 1.92	-	-	3.30 ± 2.42	3.15 ± 0.41	Group	0.26	0.04
(HOMA-IR)	WL		2.43 ± 1.88 c	-	-	3.16 ± 3.06	2.81 ± 0.41	Time	0.11	0.04
	WL+C		3.65 ± 1.81 b	-	-	3.79 ± 1.99	3.74 ± 0.40	G x T	0.59	0.02
	Time		3.00 ± 1.91	-	-	3.42 ± 2.51				
	F		2.78 ± 1.44	-	-	3.02 ± 2.08	2.90 ± 0.32	Sex	0.17	0.03
	M		3.27 ± 2.35	-	-	3.89 ± 2.90	3.56 ± 0.35	S x T	0.46	0.01
	PLA	F	2.74 ± 1.53	-	-	2.70 ± 1.62	2.72 ± 0.56	G x S	0.78	0.01
		M	3.15 ± 2.37	-	-	4.01 ± 3.07	3.58 ± 0.61	G x T x S	0.33	0.03
	WL	F	2.58 ± 1.34	-	-	2.85 ± 2.88	2.71 ± 0.54			
		M	2.23 ± 2.48 c	-	-	3.57 ± 3.40	2.90 ± 0.61			
	WL+C	F	3.03 ± 1.52	-	-	3.53 ± 1.45	3.28 ± 0.56			
		M	4.32 ± 1.92 b	-	-	4.07 ± 2.49	4.19 ± 0.58			
Leptin	PLA		41.88 ± 28.60	-	-	46.50 ± 33.74	42.44 ± 4.57	Group	0.56	0.02
(ng/mL)	WL		38.24 ± 26.78	-	-	39.83 ± 29.04	36.57 ± 4.49	Time	0.16	0.03
	WL+C		36.93 ± 25.28	-	-	36.75 ± 22.73	36.28 ± 4.45	G x T	0.43	0.03
	Time		38.97 ± 26.57	-	-	40.95 ± 28.63				
	F		54.58 ± 22.53 ♂	-	-	56.30 ± 26.97 ♂	55.44 ± 3.51 ♂	Sex	<0.001	0.41
	M		20.34 ± 17.56 ♂	-	-	22.62 ± 17.90 ♂	21.42 ± 3.84 ♂	S x T	0.84	<0.001
	PLA	F	58.81 ± 21.45 ♂	-	-	64.66 ± 31.34 ♂	61.73 ± 6.16 ♂	G x S	0.53	0.02
		M	21.56 ± 22.49 ♂	-	-	24.72 ± 22.10 ♂	23.14 ± 6.75 ♂	G x T x S	0.71	0.01
	WL	F	55.33 ± 21.57 ♂	-	-	55.55 ± 26.92 ♂	55.44 ± 5.92 ♂			
		M	16.02 ± 12.74 ♂	-	-	19.40 ± 16.54 ♂	17.71 ± 6.75 ♂			
	WL+C	F	49.55 ± 25.42 ♂	-	-	48.76 ± 21.65 ♂	49.16 ± 6.16 ♂			
		M	23.16 ± 17.18 ♂	-	-	23.64 ± 16.10 ♂	23.40 ± 6.43 ♂			

Table 10 – Continued

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Triglycerides	PLA		1.48 ± 0.72	1.35 ± 0.94	1.41 ± 1.33	1.20 ± 0.76	1.40 ± 0.20	Group	0.75	0.01
(mmol/L)	WL		1.35 ± 0.73	1.37 ± 0.90	1.20 ± 0.78	1.14 ± 0.82	1.31 ± 0.19	Time	0.07	0.04
	WL+C		1.53 ± 1.73	1.59 ± 1.23	1.42 ± 1.40	1.45 ± 1.04	1.52 ± 0.19	G x T	0.76	0.02
	Time		1.45 ± 1.15	1.44 ± 1.03	1.34 ± 1.18	1.27 ± 0.88				
	F		1.05 ± 0.44 ♂	1.02 ± 0.43 ♂	0.91 ± 0.40 ♂	1.01 ± 0.72 ♂	1.00 ± 0.15 ♂	Sex	<0.001	0.18
	M		1.93 ± 1.52 ♂	1.94 ± 1.28 ♂	1.86 ± 1.56 ♂	1.58 ± 0.96 †‡♂	1.82 ± 0.17 ♂	S x T	0.09	0.04
	PLA	F	1.13 ± 0.46	1.05 ± 0.44	0.86 ± 0.36 ♂	0.88 ± 0.33	0.98 ± 0.27 ♂	G x S	0.94	0.002
		M	1.90 ± 0.78	1.72 ± 1.24	2.08 ± 1.75 ♂‡	1.59 ± 0.96	1.82 ± 0.29 ♂	G x T x S	0.13	0.05
	WL	F	1.05 ± 0.35	1.00 ± 0.36 ♂	0.90 ± 0.26	0.86 ± 0.32	0.95 ± 0.26			
		M	1.73 ± 0.93	1.85 ± 1.16 ♂	1.60 ± 1.04	1.50 ± 1.13	1.67 ± 0.29			
	WL+C	F	0.98 ± 0.52 ♂	1.01 ± 0.53 ♂	0.98 ± 0.56	1.29 ± 1.17	1.06 ± 0.27 ♂			
		M	2.14 ± 2.35 ♂	2.22 ± 1.48 ♂	1.89 ± 1.86	1.63 ± 0.91 †	1.97 ± 0.28 ♂			
Total Cholesterol	PLA		5.07 ± 0.74	4.89 ± 0.95	4.87 ± 0.78	4.83 ± 0.90	4.92 ± 0.18	Group	0.63	0.01
(mmol/L)	WL		4.71 ± 0.89	4.88 ± 0.91	4.90 ± 1.04	4.88 ± 0.95	4.85 ± 0.18	Time	0.86	0.004
	WL+C		4.94 ± 0.83	5.10 ± 0.91	5.14 ± 0.74	5.14 ± 0.94	5.08 ± 0.17	G x T	0.11	0.05
	Time		4.90 ± 0.82	4.96 ± 0.92	4.97 ± 0.86	4.95 ± 0.93				
	F		4.82 ± 0.71	4.93 ± 0.93	4.99 ± 0.84	4.88 ± 0.95	4.91 ± 0.14	Sex	0.70	0.002
	M		5.00 ± 0.94	4.98 ± 0.92	4.94 ± 0.90	5.03 ± 0.91	4.99 ± 0.15	S x T	0.31	0.02
	PLA	F	4.95 ± 0.68	4.88 ± 1.04	4.89 ± 0.88	4.75 ± 1.04	4.87 ± 0.24	G x S	1.00	<0.001
		M	5.20 ± 0.82	4.90 ± 0.89	4.85 ± 0.69 †	4.91 ± 0.74	4.96 ± 0.26	G x T x S	0.86	0.01
	WL	F	4.63 ± 0.71	4.83 ± 0.84	4.87 ± 0.95	4.87 ± 0.82	4.80 ± 0.23			
		M	4.81 ± 1.11	4.93 ± 1.03	4.93 ± 1.21	4.89 ± 1.14	4.89 ± 0.26			
	WL+C	F	4.88 ± 0.76	5.09 ± 0.95	5.23 ± 0.70 †	5.01 ± 1.04	5.05 ± 0.24			
		M	5.00 ± 0.93	5.12 ± 0.91	5.04 ± 0.81	5.27 ± 0.84	5.11 ± 0.25			
Low Density	PLA		3.42 ± 0.84	3.26 ± 1.01	3.27 ± 0.85	3.24 ± 0.85	3.32 ± 0.18	Group	0.55	0.02
Lipoprotein	WL		3.21 ± 0.82	3.30 ± 0.84	3.35 ± 0.96	3.30 ± 0.91	3.30 ± 0.17	Time	0.99	<0.001
(U/L)	WL+C		3.45 ± 0.84	3.58 ± 0.84	3.55 ± 0.72	3.56 ± 0.95	3.54 ± 0.17	G x T	0.30	0.04
	Time		3.36 ± 0.83	3.38 ± 0.89	3.39 ± 0.84	3.37 ± 0.90				
	F		3.20 ± 0.78	3.26 ± 0.95	3.30 ± 0.89	3.19 ± 0.93	3.24 ± 0.13	Sex	0.15	0.03
	M		3.56 ± 0.85	3.52 ± 0.81	3.49 ± 0.78	3.58 ± 0.84	3.53 ± 0.15	S x T	0.37	0.02
	PLA	F	3.17 ± 0.84	3.11 ± 1.12	3.17 ± 1.01	3.07 ± 0.91	3.13 ± 0.24	G x S	0.93	0.002
		M	3.73 ± 0.76	3.45 ± 0.88	3.38 ± 0.63 †	3.44 ± 0.76	3.50 ± 0.26	G x T x S	0.58	0.02
	WL	F	3.12 ± 0.73	3.22 ± 0.83	3.26 ± 0.94	3.23 ± 0.91	3.21 ± 0.23			
		M	3.33 ± 0.94	3.42 ± 0.89	3.46 ± 1.02	3.40 ± 0.95	3.40 ± 0.26			
	WL+C	F	3.31 ± 0.83	3.47 ± 0.94	3.48 ± 0.75	3.28 ± 1.02	3.21 ± 0.24			
		M	3.61 ± 0.87	3.69 ± 0.73	3.62 ± 0.72	3.87 ± 0.81	3.70 ± 0.25			
High Density	PLA		1.35 ± 0.47	1.36 ± 0.43	1.32 ± 0.46	1.35 ± 0.47	1.32 ± 0.07	Group	0.70	0.01
Lipoprotein	WL		1.23 ± 0.39	1.30 ± 0.38	1.31 ± 0.36 †	1.35 ± 0.38 †	1.28 ± 0.07	Time	<0.01	0.07
(mmol/L)	WL+C		1.18 ± 0.36	1.21 ± 0.36	1.31 ± 0.38 †‡	1.28 ± 0.35 †	1.24 ± 0.07	G x T	0.04	0.07
	Time		1.25 ± 0.41	1.29 ± 0.39	1.31 ± 0.40 †	1.33 ± 0.40 †				
	F		1.41 ± 0.42 ♂	1.47 ± 0.37 †♂	1.51 ± 0.37 †♂	1.48 ± 0.37 †♂	1.47 ± 0.06 ♂	Sex	<0.001	0.25
	M		1.06 ± 0.31 ♂	1.07 ± 0.29 ♂	1.08 ± 0.29 ♂	1.14 ± 0.34 †♂	1.09 ± 0.06 ♂	S x T	0.13	0.03
	PLA	F	1.56 ± 0.50 ♂	1.57 ± 0.41 ♂	1.54 ± 0.47 ♂	1.51 ± 0.47 ♂	1.54 ± 0.10 ♂	G x S	0.56	0.02
		M	1.09 ± 0.30 ♂	1.10 ± 0.30 ♂	1.05 ± 0.29 ♂	1.15 ± 0.40 ♂	1.10 ± 0.11 ♂	G x T x S	0.52	0.03
	WL	F	1.30 ± 0.38	1.42 ± 0.37 †	1.43 ± 0.34 †	1.47 ± 0.35 †	1.41 ± 0.09			
		M	1.13 ± 0.40	1.14 ± 0.34	1.15 ± 0.34	1.20 ± 0.38	1.16 ± 0.11			
	WL+C	F	1.37 ± 0.36 ♂	1.42 ± 0.33 ♂	1.55 ± 0.31 †‡♂	1.47 ± 0.31 ♂	1.45 ± 0.10 ♂			
		M	0.97 ± 0.22 ♂	0.98 ± 0.23 ♂	1.04 ± 0.25 ♂	1.08 ± 0.27 †♂	1.02 ± 0.10 ♂			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Time (p=0.78), Group x Time (p=0.67), Sex x Time (p=0.34), and Group x Time x Sex (p=0.45) effects for glucose; overall Wilks' Lambda Group (p=0.93), Time (p<0.05), Group x Time (p=0.21), Sex (p<0.01), Sex x Time (p=0.14), Group x Sex (p=0.98), and Group x Time x Sex (p=0.26) effects for lipid variables; and an overall Wilks' Lambda Group (p=0.53), Time (p=0.15), Group x Time (p=0.83), Sex (p<0.01), Sex x Time (p=0.48), Group x Sex (p=0.87), and Group x Time x Sex (p=0.15) effects for hormone variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by superscripts: †=p<0.05 difference from baseline; ‡=p<0.05 difference from previous time point; ♂=p<0.05 difference between Sexes; a=p<0.05 difference from PLA; b=p<0.05 difference from WL; c= p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 11: Metabolic and Clinical Safety Markers

		Group		Weeks 0	Weeks 4	Weeks 8	Weeks 12	Mean (SEM)	Effect	p-Level	η_p^2
Clinical Markers of Muscle & Liver Function	Creatine Kinase (U/L)	PLA		130.60 ± 79.56	115.05 ± 58.17	115.20 ± 53.80	127.90 ± 91.76	126.10 ± 14.83	Group	0.89	0.004
		WL		140.08 ± 117.77	116.34 ± 67.25	148.56 ± 134.51	114.63 ± 67.63	134.54 ± 14.56	Time	0.13	0.03
		WL+C		137.84 ± 103.96	115.53 ± 72.65	151.18 ± 145.96	130.20 ± 86.89	135.04 ± 14.45	G x T	0.52	0.03
		Time		136.26 ± 100.52	115.65 ± 65.41	138.66 ± 118.79	124.19 ± 81.66				
		F		105.01 ± 96.34 ♂	88.96 ± 53.62 ♂	96.89 ± 84.86 ♂	90.97 ± 48.58 ♂	95.36 ± 11.39 ♂	Sex	<0.001	0.23
		M		173.55 ± 93.73 ♂	147.51 ± 64.64 †♂	188.51 ± 134.74 ♂‡	163.85 ± 95.26 ♂	168.43 ± 12.45 ♂	S x T	0.43	0.01
		PLA	F	102.31 ± 70.77	76.75 ± 13.71 ♂	75.98 ± 20.10	77.31 ± 20.24 ♂	83.09 ± 19.99 ♂	G x S	0.84	0.01
			M	164.56 ± 79.37	161.01 ± 57.99 ♂	162.27 ± 41.81	188.61 ± 107.88 ♂	169.11 ± 21.90 ♂	G x T x S	0.10	0.06
		WL	F	124.98 ± 139.88	91.60 ± 62.22	89.63 ± 45.87 ♂	89.86 ± 53.57	99.02 ± 19.21 ♂			
			M	159.70 ± 84.04	148.51 ± 62.12	225.18 ± 172.86 ♂‡	146.83 ± 72.92 ‡	170.06 ± 21.90 ♂			
		WL+C	F	86.07 ± 56.15 ♂	98.30 ± 68.80	125.67 ± 139.37	105.82 ± 61.14	103.97 ± 19.99 ♂			
			M	194.31 ± 116.55 ♂	134.32 ± 75.24 †	179.02 ± 154.49	156.80 ± 104.91	166.11 ± 20.88 ♂			
	Lactate Dehydrogenase (U/L)	PLA		146.01 ± 20.93	144.90 ± 21.48	146.03 ± 22.73	146.24 ± 17.36	146.11 ± 4.37	Group	0.81	0.01
		WL		146.78 ± 27.63	144.40 ± 20.27	151.35 ± 27.93 ‡	148.85 ± 23.04	148.32 ± 4.29	Time	0.07	0.04
		WL+C		145.59 ± 23.77	148.46 ± 22.63	154.97 ± 27.13 †	149.65 ± 19.77	150.02 ± 4.26	G x T	0.61	0.02
		Time		146.13 ± 23.95	145.93 ± 21.24	150.86 ± 25.95 ‡	148.28 ± 19.98				
		F		140.39 ± 20.91 ♂	141.16 ± 20.37 ♂	147.13 ± 24.99 †‡	143.79 ± 20.00 ♂	143.07 ± 3.36 ♂	Sex	0.05	0.06
		M		152.99 ± 25.83 ♂	151.63 ± 21.16 ♂	155.30 ± 26.77	153.63 ± 18.90 ♂	153.23 ± 3.67 ♂	S x T	0.74	0.01
		PLA	F	142.75 ± 19.07	141.23 ± 21.97	143.82 ± 24.56	142.80 ± 20.23	142.65 ± 5.89	G x S	0.68	0.01
			M	149.92 ± 23.37	149.30 ± 21.15	148.69 ± 21.30	150.36 ± 12.99	149.57 ± 6.45	G x T x S	0.41	0.03
		WL	F	143.71 ± 23.39	143.29 ± 22.87	148.43 ± 27.96	143.42 ± 21.45	144.71 ± 5.66			
			M	150.78 ± 33.25	145.84 ± 17.41	155.16 ± 28.91	155.92 ± 24.21	151.92 ± 6.45			
		WL+C	F	134.42 ± 20.31 ♂	138.78 ± 17.14 ♂	149.04 ± 23.87 †‡	145.18 ± 19.87 †	141.86 ± 5.89			
			M	157.77 ± 21.83 ♂	159.02 ± 23.83 ♂	161.45 ± 30.06	154.54 ± 19.37	158.19 ± 6.15			
	Alanine Aminotransferase (U/L)	PLA		27.03 ± 20.46	26.50 ± 20.15	28.42 ± 23.41	29.26 ± 17.26	28.40 ± 3.19	Group	0.86	0.005
		WL		22.89 ± 15.04	24.26 ± 14.63	26.77 ± 17.39 †	26.07 ± 16.36 †	26.02 ± 3.14	Time	0.15	0.03
		WL+C		26.43 ± 14.70	26.68 ± 13.79	26.81 ± 14.16	25.24 ± 12.42	26.55 ± 3.11	G x T	0.34	0.04
		Time		25.43 ± 16.73	25.80 ± 16.16	27.32 ± 18.37 †	26.82 ± 15.32				
		F		18.48 ± 6.78 ♂	20.33 ± 10.62 ♂	20.48 ± 9.29 ♂	21.22 ± 9.32 †♂	20.18 ± 2.45 ♂	Sex	<0.001	0.18
		M		33.72 ± 20.95 ♂	32.33 ± 19.16 ♂	35.48 ± 22.88 ♂‡	33.51 ± 18.31 ♂	33.80 ± 2.68 ♂	S x T	0.19	0.03
		PLA	F	20.13 ± 8.21	21.22 ± 11.40	21.25 ± 11.58	24.59 ± 12.56 †	21.80 ± 4.31 ♂	G x S	0.91	0.003
			M	35.31 ± 27.47	32.84 ± 26.59	37.03 ± 31.04	34.87 ± 20.93	35.01 ± 4.72 ♂	G x T x S	0.25	0.04
		WL	F	16.92 ± 4.72 ♂	17.84 ± 6.34 ♂	18.39 ± 4.50 ♂	19.45 ± 6.25 ♂	18.15 ± 4.14 ♂			
			M	30.66 ± 20.11 ♂	32.60 ± 18.24 ♂	37.67 ± 21.88 †♂	34.67 ± 21.36 ♂	33.90 ± 4.72 ♂			
		WL+C	F	18.52 ± 7.28 ♂	22.13 ± 13.56	21.98 ± 10.87	19.77 ± 8.11	20.60 ± 4.31			
			M	35.06 ± 16.13 ♂	31.63 ± 12.82	32.09 ± 15.89	31.21 ± 13.85	32.50 ± 4.50			

Table 11 – Continued

				Weeks				Mean			
	Group		0	4	8	12	(SEM)	Effect	p-Level	η_p^2
Clinical Markers of Kidney Function	Blood Urea Nitrogen (mmol/L)	PLA	4.18 ± 1.24	3.89 ± 1.01 [bc]	3.30 ± 0.77 [†‡]	3.12 ± 0.98 [†]	3.64 ± 0.16 [bc]	Group	0.07	0.08
		WL	3.63 ± 0.94	3.08 ± 0.96 [a†]	3.08 ± 0.78 [†]	2.84 ± 1.02 [†]	3.21 ± 0.15 [a]	Time	<0.001	0.35
		WL+C	3.61 ± 0.88	3.32 ± 0.83 [a]	3.01 ± 0.70 [†‡]	2.71 ± 0.73 [†‡]	3.17 ± 0.15 [a]	G x T	0.17	0.05
		Time	3.80 ± 1.05	3.42 ± 0.98 [†]	3.13 ± 0.75 [†‡]	2.88 ± 0.92 [†‡]				
		F	3.57 ± 0.87 [♂]	3.13 ± 0.76 [†♂]	2.88 ± 0.62 [†‡♂]	2.58 ± 0.61 [†‡♂]	3.05 ± 0.12 [♂]	Sex	0.00	0.15
		M	4.08 ± 1.18 [♂]	3.77 ± 1.10 [†♂]	3.42 ± 0.79 [†‡♂]	3.25 ± 1.09 [†♂]	3.64 ± 0.13 [♂]	S x T	0.81	0.00
		PLA F	3.96 ± 0.99	3.57 ± 0.87 [b]	3.11 ± 0.62 [†‡]	2.97 ± 0.60 [†]	3.40 ± 0.21 [b]	G x S	0.68	0.01
		M	4.45 ± 1.51	4.26 ± 1.07 [b]	3.52 ± 0.91 [†‡]	3.30 ± 1.32 [†]	3.88 ± 0.23	G x T x S	0.70	0.02
		WL F	3.37 ± 0.81	2.79 ± 0.59 [a†]	2.70 ± 0.46 [†♂]	2.36 ± 0.57 [†♂]	2.80 ± 0.20 [a♂]			
		M	3.97 ± 1.03	3.47 ± 1.22 [a]	3.58 ± 0.84 [♂]	3.45 ± 1.16 [♂]	3.62 ± 0.23 [♂]			
		WL+C F	3.38 ± 0.73	3.05 ± 0.62	2.85 ± 0.74 [†]	2.43 ± 0.51 [†‡]	2.80 ± 0.21			
		M	3.85 ± 1.00	3.61 ± 0.96	3.19 ± 0.63 [†]	3.02 ± 0.82 [†]	3.42 ± 0.22			
	Creatinine (µmol/L)	PLA	78.19 ± 14.48	72.22 ± 10.63 [†]	78.89 ± 17.70 [‡]	81.95 ± 14.47	78.29 ± 2.74	Group	0.40	0.03
		WL	74.94 ± 17.15	74.00 ± 18.66	75.31 ± 20.84	83.11 ± 14.01 [†‡]	78.12 ± 2.69	Time	<0.001	0.17
		WL+C	77.40 ± 18.75	79.14 ± 20.68	85.16 ± 20.32 [†‡]	87.17 ± 17.10 [†]	82.71 ± 2.67	G x T	0.18	0.05
		Time	76.82 ± 16.72	75.16 ± 17.29	79.80 ± 19.83 [‡]	84.11 ± 15.20 [†‡]				
		F	67.47 ± 12.18 [♂]	67.08 ± 13.32 [♂]	71.96 ± 17.01 [†‡♂]	76.87 ± 12.27 [†‡♂]	70.92 ± 2.10 [♂]	Sex	<0.001	0.34
		M	87.98 ± 14.49 [♂]	84.82 ± 16.67 [♂]	89.16 ± 19.11 [♂]	92.75 ± 13.93 [†♂]	88.50 ± 2.30 [♂]	S x T	0.46	0.01
		PLA F	72.13 ± 12.58 [♂]	68.71 ± 10.74	75.15 ± 19.32	76.05 ± 15.89 [♂]	73.01 ± 3.69	G x S	0.27	0.04
		M	85.47 ± 13.70 [♂]	76.43 ± 9.30 [a†]	83.38 ± 15.30	89.02 ± 8.83 [♂]	83.58 ± 4.04	G x T x S	0.72	0.02
		WL F	65.12 ± 12.84 [♂]	64.82 ± 13.94 [♂]	67.44 ± 17.98 [♂]	75.76 ± 7.73 [†‡♂]	68.29 ± 3.55 [♂]			
		M	87.71 ± 13.37 [♂]	85.93 ± 17.67 [♂]	85.55 ± 20.60 [♂]	92.66 ± 14.86 [♂]	87.96 ± 4.04 [♂]			
		WL+C F	65.36 ± 10.60 [♂]	67.88 ± 15.60 [♂]	73.67 ± 13.52 [†♂]	78.89 ± 12.96 [†♂]	71.45 ± 3.69 [♂]			
		M	90.52 ± 16.92 [♂]	91.43 ± 18.84 [a♂]	97.69 ± 19.40 [†♂]	96.21 ± 16.92 [♂]	93.96 ± 3.86 [♂]			
	BUN:Creatinine Ratio	PLA	13.71 ± 4.79	13.56 ± 3.87 [bc]	10.87 ± 3.58 [c†‡]	9.80 ± 3.68 [c†]	48.38 ± 2.33 [c]	Group	0.03	0.10
		WL	12.46 ± 3.92	10.60 ± 2.96 [a†]	10.65 ± 3.26 [†]	8.39 ± 2.36 [†‡]	42.40 ± 2.29	Time	<0.001	0.38
		WL+C	11.87 ± 2.82	10.83 ± 3.16 [a]	9.04 ± 2.39 [a†‡]	7.89 ± 2.37 [a†]	39.90 ± 2.28 [a]	G x T	0.15	0.05
		Time	12.66 ± 3.93	11.63 ± 3.56 [†]	10.18 ± 3.17 [†‡]	8.68 ± 2.93 [†‡]				
		F	13.43 ± 3.86	11.92 ± 3.44 [†]	10.37 ± 3.00 [†‡]	8.56 ± 2.67 [†‡]	44.74 ± 1.79	Sex	0.38	0.01
		M	11.75 ± 3.88	11.30 ± 3.72	9.94 ± 3.40 [†‡]	8.82 ± 3.25 [†‡]	42.38 ± 1.96	S x T	0.11	0.03
		PLA F	14.04 ± 4.54	13.11 ± 3.53	10.79 ± 3.05 [†‡]	10.11 ± 2.99 [b†]	48.51 ± 3.15	G x S	0.73	0.01
		M	13.31 ± 5.31	14.10 ± 4.37 [bc]	10.96 ± 4.30 [†‡]	9.43 ± 4.51 [†]	48.25 ± 3.45 [c]	G x T x S	0.39	0.03
		WL F	13.36 ± 4.45	11.08 ± 3.29 [†]	10.60 ± 3.47 [†]	7.76 ± 1.83 [a†‡]	43.21 ± 3.02			
		M	11.30 ± 2.93	9.97 ± 2.49 [a]	10.72 ± 3.13	9.22 ± 2.79	41.60 ± 3.45			
		WL+C F	12.88 ± 2.43	11.64 ± 3.46	9.70 ± 2.49 [†‡]	7.88 ± 2.61 [†‡]	42.51 ± 3.15			
		M	10.76 ± 2.90	9.96 ± 2.69 [a]	8.32 ± 2.15 [†]	7.89 ± 2.21 [†]	37.28 ± 3.29 [a]			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.52), Time (p<0.01), Group x Time (p=0.24), Sex (p<0.01), Sex x Time (p=0.06), and Group x Sex (p=0.57), Group x Time x Sex (p=0.43) effects for liver function related variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 12: Blood Chemistry Changes from Baseline

			PLA		WL		WL+C		
	(Normal Range)	*Baseline/Week12*	**N**	**%**	**N**	**%**	**N**	**%**	χ^2
Lipids & Glucose	Total-C	Normal/Normal	8	36%	13	57%	10	43%	0.46
	<5.2 mmol/L	Normal/High	2	9%	2	9%	5	22%	
		High/Normal	7	32%	3	13%	3	13%	
		High/High	5	23%	5	22%	5	22%	
	HDL-C	Normal/Normal	5	23%	5	22%	5	22%	0.84
	>1.45 mmol/L	Normal/High	1	5%	4	17%	3	13%	
		High/Normal	1	5%	0	0%	1	4%	
		High/High	15	68%	14	61%	14	61%	
	LDL-C	Normal/Normal	9	41%	12	52%	9	39%	0.93
	<2.59 mmol/L	Normal/High	1	5%	2	9%	2	9%	
		High/Normal	3	14%	2	9%	4	17%	
		High/High	9	41%	7	30%	8	35%	
	Triglyceride	Normal/Normal	19	86%	20	87%	20	87%	0.75
	<2.3 mmol/L	Normal/High	1	5%	0	0%	2	9%	
		High/Normal	1	5%	1	4%	0	0%	
		High/High	1	5%	2	9%	1	4%	
	Glucose	Normal/Normal	21	95%	20	87%	19	83%	0.75
	4.11-6.05 mmol/L	Normal/High	0	0%	1	4%	1	4%	
		High/Normal	1	5%	2	9%	2	9%	
		High/High	0	0%	0	0%	1	4%	
Liver	ALP	Normal/Normal	18	100%	18	86%	16	84%	0.55
	35-129 U/L	Normal/High	0	0%	2	10%	2	11%	
		High/Normal	0	0%	0	0%	0	0%	
		High/High	0	0%	1	5%	1	5%	
	ALT	Normal/Normal	16	73%	19	83%	18	78%	0.66
	10-50 U/L	Normal/High	1	5%	2	9%	1	4%	
		High/Normal	0	0%	0	0%	1	4%	
		High/High	5	23%	2	9%	3	13%	
	AST	Normal/Normal	21	95%	22	96%	22	96%	0.56
	10-50 U/L	Normal/High	0	0%	0	0%	1	4%	
		High/Normal	0	0%	0	0%	0	0%	
		High/High	1	5%	1	4%	0	0%	
Muscle	CK	Normal/Normal	15	68%	18	78%	14	61%	0.91
	26-308 U/L	Normal/High	1	5%	1	4%	2	9%	
		High/Normal	2	9%	2	9%	3	13%	
		High/High	4	18%	2	9%	4	17%	
	LDH	Normal/Normal	16	73%	15	65%	15	65%	0.98
	135-250 U/L	Normal/High	1	5%	3	13%	3	13%	
		High/Normal	2	9%	2	9%	2	9%	
		High/High	3	14%	3	13%	3	13%	
Kidney	BUN	Normal/Normal	21	95%	23	100%	23	100%	0.35
	2.14-7.14 mmol/L	Normal/High	0	0%	0	0%	0	0%	
		High/Normal	1	5%	0	0%	0	0%	
		High/High	0	0%	0	0%	0	0%	
	Creatinine	Normal/Normal	22	100%	22	96%	22	96%	0.61
	45-104 µmol/L	Normal/High	0	0%	0	0%	0	0%	
		High/Normal	0	0%	0	0%	0	0%	
		High/High	0	0%	1	4%	1	4%	

Data are presented as frequencies and percent N. Statistical significance is detailed from chi-squared analysis. Rows report total number of people that were normal or high at baseline and at week 12 (i.e. Normal/High; baseline normal, wk12 high). Percent represents the portion of total people in each group.

Whole blood. Wilks' Lambda revealed Time ($p<0.01$), Sex ($p<0.01$), and Sex x Time ($p<0.01$) but, no Group ($p=0.83$), Group x Time ($p=0.90$), Group x Sex ($p=0.52$), or Group x Time x Sex ($p=0.45$) effects for the whole blood variables, white blood cells (WBC; K/uL), lymphocytes (LYM; K/uL), MID cells [monocytes/eosinophils/basophils] (MID; K/uL), granulocytes (GRAN; K/uL), red blood cells (RBC; M/uL), hemoglobin (HGB; g/dL), hematocrit (HCT; %), mean corpuscular-volume (MCV; fL); -hemoglobin (MCH; pg); -hemoglobin concentration (MCHC; g/dL), red cell distribution width (RDW; %), platelets (PLT; K/uL), or mean platelet volume (MPV; fL). Univariate analysis indicated interaction effects of sex ($p<0.001$) for RBC, HGB, HCT, MCHC, PLT, and ($p<0.05$) MCH as well as time ($p<0.01$) for MCV, MCH, and MCHC plus, sex x time ($p<0.01$) for MCV, MCHC, ($p\leq0.05$) RBC, HGB, and MCH only. No group, group x time, or group x time x sex effects were observed among any of the whole blood variables, apart from RDW ($p\leq0.05$) with group x sex and group x sex x time effects.

Pairwise analysis showed overall sex differences in RBC (F 4.7±0.1; M 5.1±0.1 M/uL), HGB (F 13.3±0.2; M 15.2±0.2 g/dL), HCT (F 41.5±0.5; M 46.2±0.5 %), MCH (F 28.6±0.3; M 29.8±0.4 pg), MCHC (F 32.0±0.1; M 32.8±0.1 g/dL), and PLT (F 240.8±7.9; M 199.5±8.9 K/uL). WL exhibited sex differences for WBC (F 7.0±0.3; M 5.8±0.4 K/uL), GRAN (F 4.2±0.3; M 3.2±0.3 K/uL), HGB (F 13.0±0.3; M 14.8±0.3 g/dL), HCT (F 40.6±0.8; M 45.4±0.9 %), MCV (F 86.5±1.4; M 91.6±1.6 fL), MCH (F 27.6±0.5; M 29.9±0.6 pg), MCHC (F 31.9±0.2; M 32.7±0.2 g/dL), RDW (F 14.3±0.3; M 13.2±0.3 %), and PLT (F 256.2±13.3; M 199.8±15.9 K/uL). Despite some fluctuation between time points, no significant differences existed, as all measures were in normal reference ranges,

defined as; WBC 4.1-10.9 (K/uL), LYM 0.6-4.1 (K/uL), MID 0-1.8 (K/uL), GRAN 2-7.8 (K/uL), RBC 4.2-6.3 (M/uL), HGB 12-18 (g/dL), HCT 37-51 (%), MCV 80-97 (fL), MCH 26-32 (pg), MCHC 31-36 (g/dL), RDW 11.5-14.5 (%), PLT 140-440 (K/uL), MPV 0-99.8 (fL). *Table 13* presents whole blood cell count assessment data within each group.

Hemodynamics

Overall Wilks' Lambda revealed significant effects of Sex ($p<0.01$) with no Group ($p=0.24$), Time ($p=0.88$), Group x Time ($p=0.30$), Sex x Time ($p=0.52$), Group x Sex ($p=0.99$), or Group x Time x Sex ($p=0.65$) effects for the resting hemodynamic variables of heart rate (HR; bpm), systolic and diastolic blood pressure (SBP, DBP; mmHg). Univariate analysis indicated significant sex ($p<0.01$) interaction effects for HR and SBP only, with no group, time, group x time, sex x time, or group x time x sex effects for any resting hemodynamic measure. Pairwise analysis showed males generally having a lower HR (F 68±1; M 59±2) and greater SBP (F 116±2; M 123±2) at every time point. HR for WL+C also showed a significant decrease from baseline at week 8 (WL+C 67±11; WL+C 63±10 bpm). The supplement groups differed in blood pressure ($\frac{SBP}{DBP}$) at week 4 (WL+C $\frac{[124\pm16]}{[81\pm9]}$; WL $\frac{[115\pm10]}{[75\pm6]}$ mmHg) yet, only in DBP by week 12 (WL+C 80±6; WL 75±9). Although, HR and BP remained within normal ranges (HR ~60-100 bpm; BP $\frac{[90 \text{ to } 130]}{[60 \text{ to } 80]}$ mmHg) for all groups with no differences between them. *Table 14* presents resting hemodynamic data within each group.

These data reject $H_0$3: Clinical health and safety markers will improve significantly in treatment groups compared to baseline and/or placebo.

Table 13: Whole Blood Cell Counts

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
WBC	PLA		6.0 ± 1.3	6.2 ± 1.2	6.2 ± 1.3	6.0 ± 1.0	6.1 ± 0.3	Group	0.70	0.01
(K/uL)	WL		6.4 ± 1.5	6.7 ± 1.6	6.4 ± 1.6	6.5 ± 1.2	6.4 ± 0.3	Time	0.30	0.02
	WL+C		6.0 ± 1.4	6.5 ± 2.0	6.2 ± 1.7	6.2 ± 1.8	6.2 ± 0.3	G x T	0.86	0.01
	Time		6.1 ± 1.4	6.5 ± 1.6	6.3 ± 1.6	6.3 ± 1.4				
	F		6.3 ± 1.6	6.8 ± 1.9 †	6.6 ± 1.5 ♂	6.4 ± 1.6	6.5 ± 0.2	Sex	0.07	0.05
	M		6.0 ± 1.2	6.1 ± 1.3	5.8 ± 1.5 ♂	6.0 ± 1.1	6.0 ± 0.2	S x T	0.44	0.01
	PLA	F	6.4 ± 1.1	6.4 ± 1.1	6.5 ± 1.3	6.2 ± 1.1	6.4 ± 0.4	G x S	0.25	0.04
		M	5.6 ± 1.5	6.0 ± 1.3	5.9 ± 1.3	5.7 ± 0.8	5.8 ± 0.4	G x T x S	0.18	0.05
	WL	F	6.6 ± 1.8	7.3 ± 1.8 ♂	7.3 ± 1.4 ♂	6.8 ± 1.0	7.0 ± 0.3 ♂			
		M	6.2 ± 1.2	5.8 ± 0.8 ♂	5.1 ± 1.0 †♂	6.2 ± 1.4 ‡	5.8 ± 0.4 ♂			
	WL+C	F	5.8 ± 1.8	6.6 ± 2.5	6.1 ± 1.6	6.3 ± 2.4	6.2 ± 0.4			
		M	6.1 ± 0.9	6.5 ± 1.5	6.3 ± 1.9	6.1 ± 1.0	6.3 ± 0.4			
LYM	PLA		1.7 ± 0.5 b	1.9 ± 0.5	1.8 ± 0.4	1.7 ± 0.4	1.8 ± 0.1	Group	0.24	0.05
(K/uL)	WL		2.1 ± 0.5 a	2.0 ± 0.6	1.9 ± 0.5	2.0 ± 0.5	2.0 ± 0.1	Time	0.14	0.03
	WL+C		1.9 ± 0.4	2.0 ± 0.4	1.8 ± 0.5	1.9 ± 0.5	1.9 ± 0.1	G x T	0.83	0.02
	Time		1.9 ± 0.5	2.0 ± 0.5	1.8 ± 0.5 ‡	1.9 ± 0.5				
	F		1.9 ± 0.5	2.1 ± 0.5	1.9 ± 0.4 ‡	1.9 ± 0.5	1.9 ± 0.1	Sex	0.44	0.01
	M		1.9 ± 0.5	1.9 ± 0.4	1.8 ± 0.5	1.9 ± 0.5	1.8 ± 0.1	S x T	0.23	0.02
	PLA	F	1.8 ± 0.4	2.1 ± 0.5	1.9 ± 0.4	1.7 ± 0.4	1.9 ± 0.1	G x S	0.68	0.01
		M	1.6 ± 0.6	1.7 ± 0.4	1.7 ± 0.4	1.8 ± 0.3	1.7 ± 0.1	G x T x S	0.77	0.02
	WL	F	2.1 ± 0.5	2.1 ± 0.6	1.9 ± 0.4	2.0 ± 0.4	2.0 ± 0.1			
		M	2.0 ± 0.6	1.9 ± 0.6	1.9 ± 0.7	1.9 ± 0.6	2.0 ± 0.1			
	WL+C	F	1.8 ± 0.4	2.0 ± 0.5	1.8 ± 0.5	1.9 ± 0.6	1.9 ± 0.1			
		M	1.9 ± 0.3	2.0 ± 0.3	1.8 ± 0.5	2.0 ± 0.5	1.9 ± 0.1			
MID	PLA		0.6 ± 0.3 b	0.7 ± 0.4	0.5 ± 0.1 ‡	0.6 ± 0.2	0.6 ± 0.0	Group	0.14	0.06
(K/uL)	WL		0.8 ± 0.3 ac	0.7 ± 0.3	0.6 ± 0.2 †	0.7 ± 0.4	0.7 ± 0.0	Time	0.13	0.03
	WL+C		0.6 ± 0.2 b	0.6 ± 0.2	0.6 ± 0.1	0.7 ± 0.6	0.6 ± 0.0	G x T	0.53	0.03
	Time		0.7 ± 0.2	0.7 ± 0.3	0.6 ± 0.2 †‡	0.7 ± 0.4				
	F		0.7 ± 0.3	0.7 ± 0.4	0.6 ± 0.2 †‡	0.7 ± 0.3	0.7 ± 0.0	Sex	0.22	0.02
	M		0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.7 ± 0.5	0.6 ± 0.0	S x T	0.68	0.01
	PLA	F	0.7 ± 0.3	0.7 ± 0.4	0.5 ± 0.2 †‡	0.6 ± 0.3	0.6 ± 0.1	G x S	0.48	0.02
		M	0.5 ± 0.1	0.7 ± 0.3	0.5 ± 0.1	0.5 ± 0.2	0.6 ± 0.1	G x T x S	0.97	0.01
	WL	F	0.8 ± 0.3 c	0.8 ± 0.4	0.6 ± 0.2 †	0.8 ± 0.3	0.8 ± 0.0 c			
		M	0.7 ± 0.2	0.6 ± 0.2	0.6 ± 0.3	0.7 ± 0.4	0.7 ± 0.1			
	WL+C	F	0.6 ± 0.2 b	0.6 ± 0.3	0.6 ± 0.2	0.6 ± 0.4	0.6 ± 0.1 b			
		M	0.6 ± 0.2	0.6 ± 0.1	0.6 ± 0.1	0.7 ± 0.7	0.6 ± 0.1			
GRAN	PLA		3.7 ± 1.0	3.7 ± 1.2	3.9 ± 1.0	3.7 ± 0.8	3.7 ± 0.2	Group	1.00	<0.001
(K/uL)	WL		3.6 ± 1.4	3.9 ± 1.2	3.8 ± 1.5	3.8 ± 1.1	3.7 ± 0.2	Time	0.48	0.01
	WL+C		3.5 ± 1.2	3.9 ± 1.7	3.8 ± 1.5	3.6 ± 1.5	3.7 ± 0.2	G x T	0.90	0.01
	Time		3.6 ± 1.2	3.8 ± 1.4	3.8 ± 1.3	3.7 ± 1.2				
	F		3.7 ± 1.4	4.0 ± 1.6	4.2 ± 1.3 †♂	3.9 ± 1.3	3.9 ± 0.2	Sex	0.09	0.05
	M		3.5 ± 1.0	3.7 ± 1.1	3.4 ± 1.4 ♂	3.4 ± 1.0	3.5 ± 0.2	S x T	0.29	0.02
	PLA	F	3.9 ± 1.1	3.6 ± 1.2	4.1 ± 1.0	3.8 ± 0.9	3.9 ± 0.3	G x S	0.21	0.05
		M	3.4 ± 1.0	3.7 ± 1.2	3.7 ± 1.0	3.4 ± 0.6	3.6 ± 0.3	G x T x S	0.07	0.06
	WL	F	3.8 ± 1.5	4.4 ± 1.4	4.7 ± 1.2 c†♂	4.0 ± 0.7	4.2 ± 0.3 ♂			
		M	3.4 ± 1.1	3.3 ± 0.3	2.6 ± 0.8 c†♂	3.5 ± 1.4	3.2 ± 0.3 ♂			
	WL+C	F	3.4 ± 1.5	3.9 ± 2.0	3.7 ± 1.4 b	3.8 ± 1.9	3.7 ± 0.3			
		M	3.7 ± 0.8	3.9 ± 1.5	3.9 ± 1.7 b	3.4 ± 0.8	3.7 ± 0.3			

Table 13 – Continued

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
RBC	PLA		4.9 ± 0.7	4.7 ± 0.5 †	4.8 ± 0.4	4.8 ± 0.7	4.9 ± 0.1	Group	0.61	0.02
(M/uL)	WL		4.8 ± 0.4	4.8 ± 0.5	4.7 ± 0.4	4.9 ± 0.5	4.8 ± 0.1	Time	0.27	0.02
	WL+C		4.9 ± 0.5	5.0 ± 0.6	4.8 ± 0.8	5.0 ± 0.7	4.9 ± 0.1	G x T	0.47	0.03
	Time		4.9 ± 0.5	4.8 ± 0.5	4.8 ± 0.6	4.9 ± 0.6				
	F		4.6 ± 0.3 ♂	4.7 ± 0.5 ♂	4.7 ± 0.4 ♂	4.7 ± 0.7 ♂	4.7 ± 0.1 ♂	Sex	<0.001	0.28
	M		5.3 ± 0.5 ♂	5.1 ± 0.5 †♂	5.0 ± 0.7 †♂	5.1 ± 0.4 ♂	5.1 ± 0.1 ♂	S x T	0.05	0.04
	PLA	F	4.5 ± 0.3 ♂	4.4 ± 0.3 c♂	4.6 ± 0.3 ♂	4.6 ± 0.8	4.5 ± 0.1 ♂	G x S	0.21	0.05
		M	5.5 ± 0.6 b♂	5.1 ± 0.4 †♂	5.1 ± 0.4 †♂	5.1 ± 0.3 †	5.2 ± 0.1 ♂	G x T x S	0.54	0.03
	WL	F	4.7 ± 0.3 ♂	4.7 ± 0.4	4.7 ± 0.3	4.8 ± 0.7	4.7 ± 0.1			
		M	5.1 ± 0.4 a♂	5.0 ± 0.6	4.8 ± 0.5	5.0 ± 0.3	5.0 ± 0.1			
	WL+C	F	4.6 ± 0.3 ♂	4.9 ± 0.7 a†	4.7 ± 0.5	4.7 ± 0.7 ♂	4.7 ± 0.1 ♂			
		M	5.2 ± 0.4 ♂	5.1 ± 0.5	5.0 ± 1.0	5.3 ± 0.5 ♂	5.2 ± 0.1 ♂			
HGB	PLA		14.4 ± 1.9 b	13.8 ± 1.2	14.2 ± 1.2	14.2 ± 2.2	14.3 ± 0.2	Group	0.16	0.06
(g/dL)	WL		13.7 ± 1.7 a	13.7 ± 1.8	13.5 ± 1.4	14.1 ± 1.7	13.9 ± 0.2	Time	0.37	0.02
	WL+C		14.2 ± 1.5	14.7 ± 2.0	14.2 ± 2.1	14.7 ± 1.9	14.5 ± 0.2	G x T	0.42	0.03
	Time		14.1 ± 1.7	14.1 ± 1.7	14.0 ± 1.6	14.3 ± 1.9				
	F		12.9 ± 0.9 ♂	13.3 ± 1.6 †♂	13.3 ± 1.1 ♂	13.6 ± 2.0 †♂	13.3 ± 0.2 ♂	Sex	<0.001	0.48
	M		15.6 ± 1.2 ♂	15.1 ± 1.4 †♂	14.7 ± 1.9 †♂	15.3 ± 1.4 ♂	15.2 ± 0.2 ♂	S x T	0.02	0.06
	PLA	F	13.1 ± 0.7 ♂	13.0 ± 0.8 ♂	13.7 ± 1.1 ♂	13.8 ± 2.9	13.4 ± 0.3 ♂	G x S	0.99	<0.001
		M	16.1 ± 1.7 ♂	14.9 ± 0.8 †♂	15.0 ± 0.9 †♂	14.8 ± 0.4 †	15.2 ± 0.3 ♂	G x T x S	0.46	0.03
	WL	F	12.6 ± 1.1 ♂	12.9 ± 1.6 ♂	12.9 ± 1.2 ♂	13.4 ± 1.7 ♂	13.0 ± 0.3 ♂			
		M	15.2 ± 1.1 ♂	14.9 ± 1.5 ♂	14.3 ± 1.2 ♂	15.0 ± 1.1 ♂	14.8 ± 0.3 ♂			
	WL+C	F	13.0 ± 0.8 ♂	14.1 ± 2.0 †♂	13.5 ± 1.0 ♂	13.5 ± 1.1 ♂	13.5 ± 0.3 ♂			
		M	15.5 ± 0.8 ♂	15.4 ± 1.7 ♂	14.9 ± 2.8 ♂	16.0 ± 1.8 ♂	15.4 ± 0.3 ♂			
HCT	PLA		44.9 ± 5.9	42.6 ± 3.4 †	43.5 ± 3.4	43.2 ± 6.1	43.9 ± 0.6	Group	0.17	0.06
(%)	WL		42.9 ± 4.1	42.4 ± 4.5	41.8 ± 3.8	43.2 ± 4.7	43.0 ± 0.6 c	Time	0.14	0.03
	WL+C		44.8 ± 3.7	45.1 ± 5.4	43.3 ± 6.0	44.9 ± 5.8	44.6 ± 0.6 b	G x T	0.51	0.03
	Time		44.2 ± 4.6	43.4 ± 4.6	42.9 ± 4.6 †	43.8 ± 5.5				
	F		41.3 ± 2.5 ♂	41.7 ± 4.6 ♂	41.3 ± 3.1 ♂	41.7 ± 5.7 ♂	41.5 ± 0.5 ♂	Sex	<0.001	0.43
	M		47.8 ± 4.1 ♂	45.6 ± 3.7 †♂	44.8 ± 5.4 †♂	46.4 ± 4.1 ♂	46.2 ± 0.5 ♂	S x T	0.11	0.03
	PLA	F	41.6 ± 2.8 ♂	40.6 ± 2.6 c♂	42.0 ± 3.4	41.7 ± 7.8	41.4 ± 0.8 ♂	G x S	0.90	0.004
		M	49.4 ± 6.1 ♂	45.2 ± 2.2 †♂	45.6 ± 2.1 †	45.2 ± 0.9 †	46.3 ± 0.9 ♂	G x T x S	0.53	0.03
	WL	F	40.4 ± 2.5 ♂	40.3 ± 3.5 c♂	40.2 ± 3.2 ♂	41.6 ± 4.9	40.6 ± 0.8 ♂			
		M	46.6 ± 2.9 ♂	45.5 ± 4.0 ♂	44.0 ± 3.6 ♂	45.5 ± 3.4	45.4 ± 0.9 ♂			
	WL+C	F	42.1 ± 1.9 ♂	44.3 ± 6.2 ab	41.9 ± 2.7	41.9 ± 4.2 ♂	42.5 ± 0.8 ♂			
		M	47.7 ± 2.9 ♂	46.1 ± 4.5	45.0 ± 8.1	48.2 ± 5.6 ♂	46.7 ± 0.8 ♂			
MCV	PLA		91.0 ± 3.9	90.9 ± 3.8	90.5 ± 3.4	90.2 ± 3.7	90.5 ± 1.1	Group	0.52	0.02
(fL)	WL		88.8 ± 5.7	88.6 ± 5.7	88.2 ± 6.4	88.6 ± 6.4	89.0 ± 1.1	Time	0.004	0.08
	WL+C		91.2 ± 5.1	90.5 ± 5.1 †	90.3 ± 5.4 †	90.3 ± 5.6 †	90.6 ± 1.0	G x T	0.51	0.03
	Time		90.4 ± 5.0	90.0 ± 5.0 †	89.7 ± 5.3 †	89.7 ± 5.4 †				
	F		90.0 ± 5.5	89.6 ± 5.6	88.9 ± 5.9 †‡	88.9 ± 6.0 †	89.4 ± 0.8	Sex	0.34	0.02
	M		90.8 ± 4.4	90.4 ± 4.1	90.6 ± 4.1	90.7 ± 4.2	90.6 ± 0.9	S x T	0.008	0.07
	PLA	F	92.1 ± 2.5 b	92.1 ± 2.6 b	91.1 ± 2.1 b†‡	90.8 ± 2.6 b†	91.5 ± 1.4 b	G x S	0.06	0.09
		M	89.5 ± 5.1	89.3 ± 4.7	89.6 ± 4.6	89.4 ± 4.9	89.5 ± 1.6	G x T x S	0.88	0.01
	WL	F	86.8 ± 6.4 ac♂	86.6 ± 6.3 ac♂	86.1 ± 7.1 a♂	86.3 ± 7.1 a♂	86.5 ± 1.4 a♂			
		M	91.7 ± 3.0 ♂	91.6 ± 3.2 ♂	91.3 ± 3.8 ♂	91.9 ± 3.5 ♂	91.6 ± 1.6 ♂			
	WL+C	F	91.3 ± 5.5 b	90.5 ± 5.8 b	89.8 ± 6.4 †	89.8 ± 6.7 †	90.4 ± 1.4			
		M	91.1 ± 5.0	90.4 ± 4.4	90.8 ± 4.3	90.8 ± 4.3	90.8 ± 1.5			

Table 13 – Continued

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
MCH	PLA		29.1 ± 1.6	29.6 ± 1.4 †	29.6 ± 1.5 †	29.7 ± 1.4 †	29.5 ± 0.4	Group	0.43	0.03
(pg)	WL		28.3 ± 2.6	28.6 ± 2.5	28.5 ± 2.7	28.8 ± 2.6 †‡	28.8 ± 0.4	Time	<0.001	0.16
	WL+C		28.8 ± 2.0	29.4 ± 2.1 †	29.4 ± 1.8 †	29.6 ± 2.1 †	29.4 ± 0.4	G x T	0.67	0.02
	Time		28.7 ± 2.1	29.2 ± 2.1 †	29.2 ± 2.1 †	29.4 ± 2.1 †‡				
	F		28.0 ± 2.3 ♂	28.7 ± 2.2 †♂	28.7 ± 2.3 †	28.9 ± 2.4 †	28.6 ± 0.3 ♂	Sex	0.02	0.09
	M		29.6 ± 1.5 ♂	29.9 ± 1.7 ♂	29.8 ± 1.6	29.9 ± 1.4	29.8 ± 0.4 ♂	S x T	0.04	0.04
	PLA	F	29.0 ± 1.3 b	29.6 ± 0.9 b†	29.7 ± 0.9 b†	30.0 ± 1.2 b†	29.6 ± 0.5 b	G x S	0.11	0.07
		M	29.3 ± 1.9	29.5 ± 2.0	29.5 ± 2.0	29.3 ± 1.5	29.4 ± 0.6	G x T x S	0.54	0.03
	WL	F	27.2 ± 2.8 a♂	27.7 ± 2.8 a†♂	27.7 ± 3.1 a†♂	27.8 ± 2.8 a†♂	27.6 ± 0.5 a♂			
		M	29.9 ± 0.8 ♂	30.0 ± 1.1 ♂	29.6 ± 1.5 ♂	30.3 ± 1.1 ‡♂	29.9 ± 0.6 ♂			
	WL+C	F	28.1 ± 2.2	28.8 ± 2.1 †	28.9 ± 2.1 †	29.1 ± 2.6 †	28.7 ± 0.5			
		M	29.6 ± 1.6	30.1 ± 1.9	30.0 ± 1.3	30.2 ± 1.4 †	30.0 ± 0.6			
MCHC	PLA		32.0 ± 1.4	32.5 ± 0.9	32.7 ± 0.7 †	32.9 ± 0.7 †	32.6 ± 0.2	Group	0.44	0.03
(g/dL)	WL		31.8 ± 1.4	32.3 ± 1.3	32.2 ± 1.0	32.5 ± 1.0 †	32.3 ± 0.2	Time	<0.001	0.20
	WL+C		31.6 ± 1.5	32.5 ± 1.2 †	32.6 ± 0.9 †	32.8 ± 0.9 †	32.4 ± 0.2	G x T	0.58	0.03
	Time		31.8 ± 1.4	32.4 ± 1.2 †	32.5 ± 0.9 †	32.7 ± 0.9 †				
	F		31.2 ± 1.4 ♂	32.0 ± 1.1 †♂	32.3 ± 0.9 †♂	32.5 ± 1.0 †♂	32.0 ± 0.1 ♂	Sex	<0.001	0.27
	M		32.6 ± 1.0 ♂	33.0 ± 1.0 ♂	32.9 ± 0.8 ♂	33.0 ± 0.6 ♂	32.8 ± 0.1 ♂	S x T	<0.001	0.09
	PLA	F	31.5 ± 1.4 ♂	32.1 ± 0.9	32.5 ± 0.6 †	33.0 ± 0.8 †b	32.3 ± 0.2	G x S	0.28	0.04
		M	32.7 ± 1.2 ♂	33.0 ± 0.8	32.9 ± 0.8	32.7 ± 0.7	32.8 ± 0.2	G x T x S	0.70	0.02
	WL	F	31.2 ± 1.5 ♂	31.9 ± 1.4 †	32.1 ± 1.2 †	32.2 ± 1.1 a†♂	31.9 ± 0.2 ♂			
		M	32.6 ± 0.6 ♂	32.7 ± 0.8	32.5 ± 0.7	32.9 ± 0.7 ♂	32.7 ± 0.2 ♂			
	WL+C	F	30.8 ± 1.3 ♂	31.8 ± 0.9 †♂	32.2 ± 0.8 †♂	32.4 ± 1.0 †♂	31.8 ± 0.2 ♂			
		M	32.5 ± 1.2 ♂	33.3 ± 1.2 †♂	33.1 ± 0.7 ♂	33.2 ± 0.4 †♂	33.0 ± 0.2 ♂			
RDW	PLA		13.5 ± 1.2	13.4 ± 1.3	13.4 ± 1.3	13.4 ± 1.0	13.5 ± 0.2	Group	0.58	0.02
(%)	WL		13.8 ± 1.2	14.0 ± 1.5	13.7 ± 1.3	14.0 ± 1.4 ‡	13.8 ± 0.2	Time	0.22	0.02
	WL+C		13.7 ± 0.8	13.7 ± 0.9	13.6 ± 0.9	13.8 ± 1.0	13.7 ± 0.2	G x T	0.82	0.02
	Time		13.7 ± 1.1	13.7 ± 1.2	13.6 ± 1.1	13.7 ± 1.1 ‡				
	F		13.8 ± 1.2	13.9 ± 1.4	13.7 ± 1.1	13.9 ± 1.3	13.8 ± 0.2	Sex	0.21	0.03
	M		13.5 ± 0.8	13.5 ± 1.0	13.4 ± 1.2	13.6 ± 0.9	13.5 ± 0.2	S x T	0.88	0.003
	PLA	F	13.4 ± 1.1	13.2 ± 1.1 b	13.1 ± 0.6 b	13.1 ± 0.6 c	13.2 ± 0.3 b	G x S	0.03	0.11
		M	13.5 ± 1.4	13.7 ± 1.5	13.8 ± 1.8	13.9 ± 1.3	13.7 ± 0.3	G x T x S	0.05	0.07
	WL	F	14.1 ± 1.4	14.5 ± 1.6 a†♂	14.2 ± 1.3 a♂	14.5 ± 1.6 ♂	14.3 ± 0.3 a♂			
		M	13.3 ± 0.3	13.1 ± 0.8 ♂	12.9 ± 0.7 ♂	13.4 ± 0.7 ‡♂	13.2 ± 0.3 ♂			
	WL+C	F	13.8 ± 1.0	13.9 ± 1.0	13.8 ± 1.0	14.0 ± 1.2 a	13.9 ± 0.3			
		M	13.6 ± 0.6	13.6 ± 0.7	13.4 ± 0.7	13.5 ± 0.7	13.5 ± 0.3			
PLT	PLA		219.0 ± 73.1	215.3 ± 47.0	224.8 ± 60.2	218.4 ± 62.0	217.6 ± 10.5	Group	0.64	0.01
(K/uL)	WL		244.5 ± 57.8	222.2 ± 65.3	237.5 ± 67.9	228.1 ± 62.7	228.0 ± 10.4	Time	0.70	0.01
	WL+C		218.6 ± 59.8	218.6 ± 62.4	210.2 ± 58.6	216.1 ± 55.6	215.0 ± 10.0	G x T	0.70	0.02
	Time		227.4 ± 63.9	218.8 ± 58.1	224.0 ± 62.4	220.8 ± 59.4				
	F		250.6 ± 65.8 ♂	231.5 ± 64.7	246.1 ± 59.8 ♂	236.7 ± 63.4 ♂	240.8 ± 7.9 ♂	Sex	<0.001	0.17
	M		197.8 ± 48.1 ♂	202.5 ± 44.4	195.7 ± 54.5 ♂	200.6 ± 47.6 ♂	199.5 ± 8.9 ♂	S x T	0.27	0.02
	PLA	F	238.5 ± 74.8	228.8 ± 45.6	233.4 ± 68.7	220.2 ± 73.0	230.2 ± 13.8	G x S	0.58	0.02
		M	193.1 ± 65.9	197.3 ± 45.1	213.2 ± 48.1	216.1 ± 47.7	204.9 ± 15.9	G x T x S	0.46	0.03
	WL	F	270.1 ± 52.3 ♂	232.4 ± 79.2	269.6 ± 55.1 ♂	252.6 ± 58.9 ♂	256.2 ± 13.3 ♂			
		M	207.7 ± 45.7 ♂	207.6 ± 36.8	191.2 ± 59.0 ♂	192.7 ± 52.2 ♂	199.8 ± 15.9 ♂			
	WL+C	F	241.5 ± 69.8	233.3 ± 69.1	233.4 ± 51.7 ‡♂	236.0 ± 58.8	236.1 ± 13.8 ♂			
		M	193.6 ± 34.6	202.5 ± 52.6	184.9 ± 57.1 ♂	194.4 ± 44.9	193.9 ± 14.4 ♂			

Table 13 – Continued

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
MPV	PLA		10.0 ± 1.6	9.7 ± 1.1	9.9 ± 1.6	9.8 ± 1.3	9.8 ± 0.2	Group	0.33	0.04
(fL)	WL		9.5 ± 1.0	9.5 ± 0.7	9.4 ± 0.7	9.6 ± 0.8	9.5 ± 0.2	Time	0.96	0.00
	WL+C		9.8 ± 1.1	10.0 ± 1.1	9.9 ± 1.1	10.1 ± 1.2	9.9 ± 0.2	G x T	0.57	0.03
	Time		9.8 ± 1.3	9.8 ± 1.0	9.7 ± 1.2	9.8 ± 1.1				
	F		9.9 ± 1.3	9.7 ± 1.0	9.7 ± 1.0	10.0 ± 1.2	9.8 ± 0.2	Sex	0.49	0.01
	M		9.6 ± 1.2	9.8 ± 1.0	9.7 ± 1.5	9.6 ± 1.0	9.7 ± 0.2	S x T	0.19	0.03
	PLA	F	10.3 ± 1.6	9.5 ± 1.0 †	9.9 ± 1.0	10.0 ± 1.4	9.9 ± 0.3	G x S	0.42	0.03
		M	9.7 ± 1.7	9.9 ± 1.2	10.0 ± 2.3	9.5 ± 1.2	9.8 ± 0.3	G x T x S	0.55	0.03
	WL	F	9.4 ± 1.1	9.5 ± 0.7	9.2 ± 0.7 [c]	9.6 ± 1.0	9.4 ± 0.3 [c]			
		M	9.5 ± 0.8	9.6 ± 0.8	9.7 ± 0.7	9.6 ± 0.4	9.6 ± 0.3			
	WL+C	F	10.1 ± 1.0	10.2 ± 1.1	10.2 ± 1.1 [b]	10.4 ± 1.2	10.2 ± 0.3 [b]			
		M	9.5 ± 1.2	9.8 ± 1.1	9.6 ± 1.2	9.7 ± 1.2	9.6 ± 0.3			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.83), Time (p<0.01), Group x Time (p=0.90), Sex (p<0.01), Sex x Time (p<0.01), and Group x Sex (p=0.52), Group x Time x Sex (p=0.45) effects for whole blood variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♀ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 14: Resting Hemodynamics

	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Heart Rate	PLA		62 ± 13	62 ± 12	63 ± 14	61 ± 11	62 ± 2	Group	0.44	0.03
(bpm)	WL		64 ± 8	63 ± 10	66 ± 10	63 ± 8	64 ± 2	Time	0.73	0.01
	WL+C		67 ± 11	66 ± 10	63 ± 10 †	65 ± 10	65 ± 2	G x T	0.17	0.05
	Time		65 ± 11	64 ± 11	64 ± 12	63 ± 10				
	F		69 ± 9 ♂	67 ± 9 ♂	67 ± 12 ♂	68 ± 9 ♂	68 ± 1 ♂	Sex	<0.001	0.20
	M		60 ± 11 ♂	60 ± 11 ♂	60 ± 10 ♂	58 ± 9 ♂	59 ± 2 ♂	S x T	0.53	0.01
	PLA	F	68 ± 10 ♂	67 ± 10 ♂	67 ± 14	66 ± 8 ♂	67 ± 2 ♂	G x S	0.79	0.01
		M	56 ± 14 ♂	57 ± 12 ♂	59 ± 14	55 ± 11 ♂	57 ± 3 ♂	G x T x S	0.17	0.05
	WL	F	68 ± 8	67 ± 10	70 ± 10 ♂	65 ± 9	67 ± 2 ♂			
		M	60 ± 7	59 ± 8	61 ± 8 ♂	61 ± 8	60 ± 3 ♂			
	WL+C	F	71 ± 11 ♂	67 ± 10	65 ± 11 †	71 ± 8 ‡♂	67 ± 2			
		M	63 ± 10 ♂	64 ± 10	60 ± 9	59 ± 9 ♂	62 ± 3			
Systolic Blood	PLA		120 ± 11	120 ± 11	118 ± 10	118 ± 11	119 ± 2	Group	0.15	0.06
Pressure	WL		117 ± 10	115 ± 10 c	118 ± 11	117 ± 12	117 ± 2 c	Time	0.67	0.01
(mmHg)	WL+C		123 ± 15	124 ± 16 b	121 ± 13	122 ± 13	123 ± 2 b	G x T	0.75	0.02
	Time		120 ± 12	120 ± 13	119 ± 11	119 ± 12				
	F		115 ± 8 ♂	116 ± 12 ♂	116 ± 10 ♂	116 ± 11 ♂	116 ± 2 ♂	Sex	<0.01	0.14
	M		126 ± 14 ♂	124 ± 13 ♂	122 ± 12 ♂	123 ± 12 †♂	123 ± 2 ♂	S x T	0.24	0.02
	PLA	F	116 ± 8	116 ± 12	114 ± 9 ♂	115 ± 11	115 ± 3 ♂	G x S	0.88	0.004
		M	125 ± 12	124 ± 8	123 ± 8 ♂	122 ± 10	123 ± 3 ♂	G x T x S	0.80	0.02
	WL	F	112 ± 7 ♂	113 ± 11	117 ± 13	114 ± 12	114 ± 3			
		M	123 ± 11 ♂	118 ± 8	119 ± 9	120 ± 12	120 ± 3			
	WL+C	F	117 ± 9 ♂	120 ± 13	118 ± 9	118 ± 10	118 ± 3 ♂			
		M	129 ± 18 ♂	128 ± 18	125 ± 15	126 ± 15	127 ± 3 ♂			
Diastolic Blood	PLA		78 ± 8	77 ± 6	79 ± 6	77 ± 7	78 ± 1	Group	0.06	0.09
Pressure	WL		76 ± 5	75 ± 6 c	76 ± 6	75 ± 9 c	76 ± 1 c	Time	0.65	0.01
(mmHg)	WL+C		80 ± 7	81 ± 9 b	79 ± 6	80 ± 6 b	80 ± 1 b	G x T	0.40	0.03
	Time		78 ± 7	78 ± 8	78 ± 6	77 ± 7				
	F		77 ± 6	77 ± 7	78 ± 6	77 ± 8	77 ± 1	Sex	0.78	0.001
	M		79 ± 8	78 ± 8	78 ± 6	77 ± 7	78 ± 1	S x T	0.76	0.01
	PLA	F	78 ± 7	77 ± 8	77 ± 6	77 ± 8	77 ± 2	G x S	0.88	0.004
		M	78 ± 10	77 ± 3	81 ± 5 b	76 ± 7 ‡	78 ± 2	G x T x S	0.54	0.03
	WL	F	76 ± 6	76 ± 8	77 ± 7	75 ± 9	76 ± 2			
		M	77 ± 4	75 ± 5 c	75 ± 6 a	74 ± 8	75 ± 2			
	WL+C	F	79 ± 7	80 ± 7	79 ± 4	80 ± 6	79 ± 2			
		M	81 ± 8	82 ± 12 b	78 ± 7	79 ± 5	80 ± 2			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.24), Time (p=0.88), Group x Time (p=0.30), Sex (p<0.01), Sex x Time (p=0.52), and Group x Sex (p=0.99), Group x Time x Sex (p=0.65) effects for resting hemodynamic variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Psychosocial Evaluation

Questionnaires

Hunger/Satiety. Overall Wilks' Lambda revealed effects of Sex ($p<0.01$) and Group x Time x Sex ($p=0.06$), with no Group ($p=0.53$), Time ($p=0.34$), Group x Time ($p=0.20$), Sex x Time ($p=0.21$), or Group x Sex ($p=0.23$) effects for hunger and satiety variables. Univariate analysis indicated sex ($p\leq0.05$) interactions effects for amount of energy and diet quality, with no group, time, group x time, sex x time, or group x time x sex effects among any of the variables.

Pairwise analysis showed overall sex differences in appetite (F 5.5±0.2; M 6.4±0.2), satisfaction from food (F 6.4±0.2; M 7.3±0.2), amount of energy (F 5.8±0.2; M 6.4±0.2), and diet quality (F 5.4±0.2; M 6.0±0.2) where men had overall greater values (*Table 15*). Moreover, compared to baseline, WL had a greater reported appetite (WL 5.3±2.2; Wk12 6.2±1.6), satisfaction from food (WL 6.2±1.3; Wk8 7.0±1.5), feeling of fullness (WL 6.2±1.7; Wk8 7.1±1.2; Wk12 7.1±1.6), and females were less hungry (WL 5.5±1.7; Wk12 4.5±1.9). WL+C females also reported being less hungry than baseline (WL+C 5.0±1.0; Wk12 4.5±1.7). Subsequently, females in the supplement groups had significantly lower reported hunger than PLA females, at week 12 (PLA 6.1±1.2; WL 4.5±1.9; WL+C 4.5±1.7). Lastly, WL+C saw a decrease from baseline for satisfaction from food at weeks 4 and 8, followed by an increase at week 12 (WL+C 7.1±1.5; Wk4 6.3±1.8; Wk8 6.1±1.4; Wk12 6.8±1.4). These data fail to reject $H_0$6: Reported hunger and satiety will significantly decrease and increase, respectively, in treatment groups compared to baseline and/or placebo.

Sleep Quality. Overall Wilks' Lambda revealed Group ($p<0.05$) but, no Time ($p=0.09$), Group x Time ($p=0.39$), Sex ($p=0.20$), Sex x Time ($p=0.53$), Group x Sex ($p=0.66$), or Group x Time x Sex ($p=0.82$) effects for sleep quality questionnaire variables. Univariate analysis indicated group ($p=0.03$) effects for hours of sleep only, with no time, group x time, sex, sex x time, or group x time x sex effects among the sleep quality variables.

Pairwise analysis indicated WL fell asleep faster compared to baseline at weeks 8 and 12 (WL 18.85±18.02; Wk8 13.67±13.70; Wk12 13.83±10.65 min). WL+C went to sleep later and took longer than PLA at week 4 (PLA 11.32±7.78; WL+C 29.02±47.52 min) and week 12 (PLA 10.93±7.40; WL+C 18.22±13.48 min). *Tables 16-16.1* shows sleep quality and Chi square analysis of values observed by week. This analysis indicated a difference between groups in; bathroom use at night at week 12 ($p=0.03$ [PLA 41; WL 13; WL+C 48 %]); nighttime coughing or snoring at week 4 ($p=0.02$ [PLA 0; WL 22; WL+C 4 %]); feeling too hot while sleeping at week 8 ($p=0.02$ [PLA 9; WL 13; WL+C 39 %]); and unspecified other reasons at baseline ($p=0.04$ [PLA 23; WL 9; WL+C 0%]). No other significant differences were observed for sleep quality values among treatments. These data reject $H_0$7: Reported sleep quality in treatment groups will not significantly differ from baseline and/or placebo.

Side Effects. *Tables 17-18* shows Chi square analysis of symptom frequency and severity values observed by week. This analysis had no significant differences among treatments. These data fail to reject $H_0$8: Reported side effects in treatment groups will not significantly differ from baseline and/or placebo.

Table 15: Hunger and Satiety Questionnaire

Variable	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Appetite	PLA		6.2 ± 1.3	6.0 ± 1.2	6.0 ± 1.6	6.3 ± 1.4	6.2 ± 0.2	Group	0.44	0.03
	WL		5.3 ± 2.2	5.5 ± 1.6	5.9 ± 1.4	6.2 ± 1.6 †	5.8 ± 0.2	Time	0.32	0.02
	WL+C		6.0 ± 1.5	5.6 ± 1.6	5.9 ± 1.3 ‡	5.7 ± 1.4	5.8 ± 0.2	G x T	0.37	0.03
	Time		5.8 ± 1.7	5.7 ± 1.5	5.9 ± 1.5	6.1 ± 1.5				
	F		5.5 ± 1.7	5.4 ± 1.4 ♂	5.6 ± 1.5 ♂	5.5 ± 1.5 ♂	5.5 ± 0.2 ♂	Sex	0.001	0.16
	M		6.2 ± 1.8	6.1 ± 1.4 ♂	6.4 ± 1.3 ♂	6.8 ± 1.2 ♂	6.4 ± 0.2 ♂	S x T	0.40	0.02
	PLA	F	6.3 ± 1.4	5.6 ± 1.2	5.6 ± 1.7	5.8 ± 1.4 ♂	5.8 ± 0.3	G x S	0.65	0.01
		M	6.2 ± 1.4	6.6 ± 1.0	6.5 ± 1.4	6.9 ± 1.2 ♂	6.6 ± 0.3	G x T x S	0.13	0.05
	WL	F	5.0 ± 2.2	5.0 ± 1.8 ♂	5.2 ± 1.3 ♂	5.7 ± 1.7 ♂	5.2 ± 0.3 ♂			
		M	5.8 ± 2.3	6.2 ± 1.0 ♂	6.9 ± 1.0 †♂	6.9 ± 1.2 †♂	6.4 ± 0.3 ♂			
	WL+C	F	5.4 ± 1.2	5.5 ± 1.3	6.0 ± 1.5	5.0 ± 1.3 ‡♂	5.5 ± 0.3			
		M	6.5 ± 1.6	5.7 ± 1.9	5.8 ± 1.2	6.5 ± 1.1 ‡♂	6.1 ± 0.3			
Hunger	PLA		5.5 ± 1.7	5.6 ± 1.7	5.6 ± 2.0	6.0 ± 1.3	5.7 ± 0.3	Group	0.66	0.01
	WL		5.6 ± 1.6	5.1 ± 1.7	5.3 ± 2.0	5.5 ± 2.1	5.4 ± 0.3	Time	0.31	0.02
	WL+C		5.6 ± 1.5	5.0 ± 1.6	5.8 ± 1.3	5.1 ± 1.6	5.4 ± 0.2	G x T	0.41	0.03
	Time		5.6 ± 1.6	5.2 ± 1.7	5.6 ± 1.8	5.5 ± 1.7				
	F		5.4 ± 1.3	5.1 ± 1.6	5.5 ± 1.7	5.0 ± 1.8 ♂	5.3 ± 0.2	Sex	0.09	0.05
	M		5.8 ± 1.9	5.4 ± 1.7	5.7 ± 1.9	6.1 ± 1.5 ♂	5.8 ± 0.2	S x T	0.18	0.03
	PLA	F	5.7 ± 1.1	5.6 ± 1.5	5.8 ± 1.6	6.1 ± 1.2 bc	5.8 ± 0.3	G x S	0.30	0.04
		M	5.4 ± 2.3	5.6 ± 1.9	5.5 ± 2.5	6.0 ± 1.3	5.6 ± 0.4	G x T x S	0.53	0.03
	WL	F	5.5 ± 1.7	4.8 ± 1.9	5.1 ± 2.1	4.5 ± 1.9 a♂	5.0 ± 0.3			
		M	5.8 ± 1.6	5.5 ± 1.3	5.6 ± 2.0	6.7 ± 1.9 ‡♂	5.9 ± 0.4			
	WL+C	F	5.0 ± 1.0	4.8 ± 1.2	5.8 ± 1.5	4.5 ± 1.7 a‡♂	5.0 ± 0.3			
		M	6.2 ± 1.7	5.1 ± 2.1	5.9 ± 1.1	5.8 ± 1.2 ♂	5.8 ± 0.4			
Satisfaction from Food	PLA		7.3 ± 1.0 b	7.3 ± 1.1 bc	7.1 ± 1.4 c	7.1 ± 1.3	7.2 ± 0.2 bc	Group	0.07	0.08
	WL		6.2 ± 1.3 ac	6.3 ± 1.4 a	7.0 ± 1.5 c†‡	6.8 ± 1.6	6.6 ± 0.2 a	Time	0.33	0.02
	WL+C		7.1 ± 1.5 b	6.3 ± 1.8 a†	6.1 ± 1.4 ab†	6.8 ± 1.4 ‡	6.6 ± 0.2 a	G x T	0.004	0.10
	Time		6.9 ± 1.4	6.6 ± 1.5	6.8 ± 1.5	6.9 ± 1.4				
	F		6.4 ± 1.3 ♂	6.5 ± 1.4	6.2 ± 1.7 ♂	6.5 ± 1.3 ♂	6.4 ± 0.2 ♂	Sex	<0.001	0.17
	M		7.4 ± 1.3 ♂	6.8 ± 1.6 †	7.4 ± 0.9 ‡♂	7.4 ± 1.4 ♂	7.3 ± 0.2 ♂	S x T	0.15	0.03
	PLA	F	7.2 ± 0.7 b	7.1 ± 1.0	6.8 ± 1.7 c	6.6 ± 1.2	6.9 ± 0.3 c	G x S	0.69	0.01
		M	7.6 ± 1.3	7.5 ± 1.2	7.6 ± 0.7	7.7 ± 1.3	7.6 ± 0.3	G x T x S	0.67	0.02
	WL	F	5.7 ± 1.3 a♂	6.2 ± 1.3	6.6 ± 1.7 c†	6.6 ± 1.3 †	6.3 ± 0.3			
		M	6.9 ± 1.2 ♂	6.5 ± 1.4	7.6 ± 1.1 ‡	7.1 ± 2.0	7.0 ± 0.3			
	WL+C	F	6.5 ± 1.5 ♂	6.2 ± 1.8	5.3 ± 1.3 ab†‡♂	6.2 ± 1.5 ‡♂	6.0 ± 0.3 a♂			
		M	7.8 ± 1.2 ♂	6.5 ± 1.9 †	7.0 ± 1.0 ♂	7.5 ± 1.0 ♂	7.2 ± 0.3 ♂			
Feeling of Fullness	PLA		6.8 ± 1.4	7.2 ± 1.5	7.1 ± 1.1	7.0 ± 1.4	7.0 ± 0.2	Group	0.58	0.02
	WL		6.2 ± 1.7	6.6 ± 1.6	7.1 ± 1.2 †	7.1 ± 1.6 †	6.7 ± 0.2	Time	0.49	0.01
	WL+C		6.9 ± 1.9	6.8 ± 1.6	6.4 ± 1.8	6.7 ± 1.3	6.7 ± 0.2	G x T	0.16	0.05
	Time		6.6 ± 1.7	6.8 ± 1.6	6.9 ± 1.4	6.9 ± 1.4				
	F		6.4 ± 1.6	6.7 ± 1.7	6.7 ± 1.5	6.8 ± 1.3	6.6 ± 0.2	Sex	0.20	0.03
	M		6.8 ± 1.8	7.0 ± 1.4	7.1 ± 1.2	7.0 ± 1.5	7.0 ± 0.2	S x T	0.99	<0.001
	PLA	F	7.0 ± 1.0	7.6 ± 1.3 bc	6.9 ± 0.9	6.9 ± 1.1	7.1 ± 0.3 c	G x S	0.16	0.06
		M	6.5 ± 1.8	6.8 ± 1.6	7.3 ± 1.3	7.0 ± 1.8	6.9 ± 0.3	G x T x S	0.46	0.03
	WL	F	6.1 ± 1.5	6.2 ± 1.8 a	7.0 ± 1.4	7.2 ± 1.6 †	6.6 ± 0.3			
		M	6.3 ± 2.0	7.0 ± 1.3	7.2 ± 1.0	7.0 ± 1.7	6.9 ± 0.3			
	WL+C	F	6.3 ± 2.1	6.3 ± 1.8 a	6.1 ± 2.0	6.2 ± 1.1	6.2 ± 0.3 a♂			
		M	7.5 ± 1.4	7.3 ± 1.3	6.7 ± 1.4	7.2 ± 1.3	7.2 ± 0.3 ♂			

Table 15 – Continued

Variable	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Amount of Energy	PLA		5.8 ± 1.5	6.4 ± 1.7	6.1 ± 1.5	5.7 ± 1.6	6.0 ± 0.3	Group	0.66	0.01
	WL		6.1 ± 1.5	6.2 ± 1.3	6.6 ± 1.4	6.3 ± 1.7	6.3 ± 0.3	Time	0.61	0.01
	WL+C		6.0 ± 1.6	5.9 ± 2.0	5.8 ± 1.7	6.1 ± 2.0	6.0 ± 0.2	G x T	0.40	0.03
	Time		5.9 ± 1.5	6.1 ± 1.7	6.2 ± 1.5	6.1 ± 1.7				
	F		5.6 ± 1.6	5.9 ± 1.6	6.2 ± 1.5	5.6 ± 1.8 ‡♂	5.8 ± 0.2 ♂	Sex	0.05	0.06
	M		6.3 ± 1.4	6.4 ± 1.8	6.2 ± 1.6	6.6 ± 1.5 ♂	6.4 ± 0.2 ♂	S x T	0.17	0.03
	PLA	F	5.3 ± 1.4 b♂	5.9 ± 1.7	6.1 ± 1.3	5.3 ± 1.4	5.6 ± 0.3	G x S	0.08	0.08
		M	6.5 ± 1.4 ♂	6.9 ± 1.7	6.2 ± 1.8	6.2 ± 1.8	6.4 ± 0.4	G x T x S	0.22	0.04
	WL	F	6.5 ± 1.6 ac	6.3 ± 1.3	6.7 ± 1.5	6.2 ± 1.9	6.4 ± 0.3 c			
		M	5.5 ± 1.2 c	6.1 ± 1.4	6.5 ± 1.4	6.5 ± 1.4	6.1 ± 0.4			
	WL+C	F	5.1 ± 1.4 b♂	5.5 ± 1.7	5.7 ± 1.6	5.2 ± 2.0 ♂	5.4 ± 0.3 b♂			
		M	6.9 ± 1.4 b♂	6.3 ± 2.2	6.0 ± 1.9	7.2 ± 1.3 ‡♂	6.6 ± 0.4 ♂			
Overall Quality of Diet	PLA		5.5 ± 1.3	5.8 ± 1.7	6.2 ± 1.6	6.2 ± 1.5	6.0 ± 0.3	Group	0.37	0.03
	WL		5.4 ± 2.0	5.4 ± 1.6	5.7 ± 1.7	5.8 ± 2.0	5.6 ± 0.3	Time	0.22	0.02
	WL+C		5.5 ± 2.0	5.4 ± 1.6	5.3 ± 1.7	5.7 ± 1.6	5.5 ± 0.3	G x T	0.79	0.02
	Time		5.5 ± 1.8	5.5 ± 1.6	5.7 ± 1.7	5.9 ± 1.7				
	F		5.1 ± 1.6 ♂	5.4 ± 1.4	5.4 ± 1.6	5.7 ± 1.5 †	5.4 ± 0.2 ♂	Sex	0.05	0.06
	M		6.0 ± 1.9 ♂	5.8 ± 1.9	6.1 ± 1.7	6.1 ± 1.9	6.0 ± 0.2 ♂	S x T	0.62	0.01
	PLA	F	5.0 ± 1.0	4.9 ± 1.4 ♂	5.5 ± 1.4 ♂	5.8 ± 1.5	5.3 ± 0.4 ♂	G x S	0.07	0.08
		M	6.2 ± 1.5	6.9 ± 1.4 bc♂	7.0 ± 1.3 b♂	6.7 ± 1.4	6.7 ± 0.4 b♂	G x T x S	0.28	0.04
	WL	F	5.1 ± 1.7	5.8 ± 1.3	5.9 ± 1.8	6.1 ± 1.7 †	5.7 ± 0.4			
		M	5.8 ± 2.3	4.9 ± 1.7 a	5.4 ± 1.7 a	5.5 ± 2.3	5.4 ± 0.4 a			
	WL+C	F	5.1 ± 2.0	5.3 ± 1.2	4.8 ± 1.4	5.3 ± 1.3	5.7 ± 0.4			
		M	6.0 ± 2.0	5.5 ± 2.0 a	5.9 ± 1.9	6.2 ± 1.8	5.9 ± 0.4			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group (p=0.53), Time (p=0.34), Group x Time (p=0.20), Sex (p<0.01), Sex x Time (p=0.21), and Group x Sex (p=0.23), Group x Time x Sex (p=0.06) effects for hunger and satiety questionnaire variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = p<0.05 difference from baseline value; ‡ = p<0.05 difference from previous time point; ♂ = p<0.05 difference between Sexes; a = p<0.05 difference from PLA; b = p<0.05 difference from WL; c = p<0.05 difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 16: Sleep Quality Index

Variable	Group		Weeks 0	4	8	12	Mean (SEM)	Effect	p-Level	η_p^2
Bed Time	PLA		22:51±00:54	22:36±00:52[c]	22:45±00:53	22:37±00:41[c]	22:44±00:11[c]	Group	0.09	0.07
(00:00 - hr:min)	WL		23:21±01:36	23:01±01:05	23:13±01:10	23:11±01:14	23:13±00:11	Time	0.46	0.01
	WL+C		23:14±01:09	23:14±01:03[a]	23:06±01:14	23:33±01:08[a‡]	23:17±00:11[a]	G x T	0.48	0.03
	Time		23:09±01:15	22:58±01:01	23:01±01:07	23:07±01:06				
	F		23:02±01:21	22:41±00:55♂	22:42±01:03♂	22:53±01:06♂	22:49±00:08♂	Sex	0.02	0.08
	M		23:16±01:08	23:17±01:04♂	23:24±01:05♂	23:24±01:04♂	23:20±00:09♂	S x T	0.31	0.02
	PLA	F	22:28±00:44	22:20±00:43	22:20±00:46♂	22:20±00:39[c]	22:22±00:15[c]	G x S	0.71	0.01
		M	23:18±00:55	22:57±00:57	23:15±00:47♂	22:58±00:34	23:07±00:16	G x T x S	0.55	0.03
	WL	F	23:20±01:54	22:45±01:03†	23:01±01:18	22:50±01:06	22:59±00:14			
		M	23:22±01:13	23:24±01:06	23:32±00:58	23:37±01:18	23:28±00:16			
	WL+C	F	23:17±01:00	23:00±00:53	22:45±00:57	23:30±01:12[a‡]	23:08±00:15[a]			
		M	23:10±01:20	23:30±01:10	23:29±01:26	23:36±01:08	23:26±00:16			
Time to Fall	PLA		13.86±12.24	11.32±7.78 [c]	12.93±8.28	10.93±7.40 [c]	12.45±2.99 [c]	Group	0.14	0.06
Asleep	WL		18.85±18.02	16.57±12.48	13.67±13.70†	13.83±10.65†	15.76±2.94	Time	0.23	0.02
(minutes)	WL+C		17.35±12.80	29.02±47.52[a†]	19.52±15.10	18.22±13.48[a]	20.86±2.92 [a]	G x T	0.22	0.05
	Time		16.73±14.55	19.08±29.45	15.41±12.92	14.38±11.09				
	F		15.43±13.17	20.32±38.20	16.62±13.40	14.81±12.17	16.83±2.30	Sex	0.78	0.001
	M		18.27±16.13	17.60±13.51	13.97±12.37	13.85±9.82 †	15.88±2.51	S x T	0.50	0.01
	PLA	F	10.83±6.69	9.25±5.04 [c]	11.79±7.64	9.58±7.89 [c]	10.36±4.03 [c]	G x S	0.36	0.03
		M	17.50±16.37	13.80±9.89	14.30±9.21	12.55±6.79	14.54±4.42	G x T x S	0.42	0.03
	WL	F	17.00±16.07	14.69±10.59	17.00±16.12	13.31±8.72	15.50±3.88			
		M	21.25±20.92	19.00±14.82	9.35±8.71 †	14.50±13.22	16.03±4.42			
	WL+C	F	18.33±14.35	37.50±64.30[a†]	21.04±14.12‡	21.67±16.00[a]	24.64±4.03 [a]			
		M	16.27±11.47	19.77±15.51	17.86±16.62	14.45±9.38	17.09±4.21			
Waking Time	PLA		06:53±00:46	06:49±00:55	06:37±00:55	07:00±01:11	06:30±00:09	Group	0.26	0.04
(00:00 - hr:min)	WL		06:45±01:07	06:21±01:01†	06:25±01:02	06:24±01:01	06:30±00:09	Time	0.24	0.02
	WL+C		06:28±00:43	06:30±00:50	06:27±00:39	06:30±00:52‡	06:50±00:09	G x T	0.43	0.03
	Time		06:42±00:53	06:33±00:56	06:30±00:52	06:38±01:03				
	F		06:34±00:51	06:27±01:01	06:23±01:00	06:21±00:57♂	06:27±00:07	Sex	0.08	0.05
	M		06:51±00:55	06:41±00:50	06:38±00:42	06:58±01:05‡♂	06:47±00:08	S x T	0.26	0.02
	PLA	F	06:56±00:42[c]	07:02±00:58[c]	06:40±01:08	06:47±01:09	06:11±00:13♂	G x S	0.31	0.04
		M	06:50±00:52	06:35±00:51	06:35±00:42	07:13±01:15	06:50±00:14♂	G x T x S	0.68	0.02
	WL	F	06:36±01:06	06:10±01:01[c†]	06:20±01:11	06:06±00:49	06:18±00:12			
		M	06:55±01:10	06:35±01:01	06:35±00:49	06:47±01:10	06:42±00:14			
	WL+C	F	06:10±00:31[a]	06:10±00:52[ab]	06:11±00:34	06:12±00:48	06:51±00:13[a]			
		M	06:49±00:47	06:53±00:39	06:46±00:37	06:52±00:50‡	06:48±00:13			
Hours Sleeping	PLA		7.09±1.35	6.80±0.97	6.95±0.75 [b]	7.09±0.87 [b]	6.98±0.17 [b]	Group	0.03	0.10
Nightly	WL		6.48±1.20	6.47±0.82	6.37±0.87 [a]	6.28±1.19 [a]	6.38±0.16 [a]	Time	0.14	0.03
(hours)	WL+C		6.87±1.02	6.26±1.00 †	6.48±1.07	6.54±1.16	6.53±0.16	G x T	0.61	0.02
	Time		6.81±1.21	6.50±0.94 †	6.60±0.93	6.63±1.12				
	F		6.78±1.10	6.61±0.96	6.75±0.90	6.69±1.13	6.71±0.13	Sex	0.39	0.01
	M		6.84±1.34	6.37±0.92 †	6.41±0.95 †	6.56±1.12	6.55±0.14	S x T	0.54	0.01
	PLA	F	7.00±1.03	6.75±1.16	7.02±0.79	7.13±0.96	6.97±0.23	G x S	0.78	0.008
		M	7.20±1.72	6.85±0.75	6.88±0.74	7.05±0.80 [b]	6.99±0.25 [b]	G x T x S	0.66	0.02
	WL	F	6.42±1.34	6.63±0.93	6.54±0.95	6.54±1.14	6.53±0.22			
		M	6.55±1.07	6.25±0.63	6.15±0.75	5.95±1.21 [a]	6.23±0.25 [a]			
	WL+C	F	6.96±0.84	6.46±0.84	6.71±0.96	6.42±1.24	6.64±0.23			
		M	6.77±1.23	6.05±1.15 †	6.23±1.17	6.68±1.10	6.43±0.24			

Data are expressed as means ± standard deviations for the placebo (PLA), weight loss formula (WL), and weight loss formula with caffeine (WL+C); M=male, F=female; Partial ETA^2 (η_p^2). General Linear Model analysis revealed overall Wilks' Lambda Group ($p<0.05$), Time ($p=0.09$), Group x Time ($p=0.39$), Sex ($p=0.20$), Sex x Time ($p=0.53$), and Group x Sex ($p=0.66$), Group x Time x Sex ($p=0.82$) effects for sleep quality questionnaire variables. Greenhouse-Geisser univariate p-levels are listed for Group (G), Time (T), Sex (S), Group x Time (G x T), Sex x Time (S x T), Group x Sex (G x S), Group x Time x Sex (G x T x S) interaction effects. Pairwise comparison is indicated by the following superscripts: † = $p<0.05$ difference from baseline value; ‡ = $p<0.05$ difference from previous time point; ♂ = $p<0.05$ difference between Sexes; a = $p<0.05$ difference from PLA; b = $p<0.05$ difference from WL; c = $p<0.05$ difference from WL+C. LSD post hoc analysis was used to show group differences, indicated by subscripts a, b, and c, for group means only (excluding Time and Sex data), on the above table.

Table 16.1 – Sleep Quality Index Continued (Frequency data)

		0		4		8		12			
Variable	**Group**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	χ^2	
Cannot Sleep within 30 min?	PLA	2	9%	0	0%	1	5%	1	5%	*Week 0*	0.27
	WL	6	26%	3	13%	4	17%	2	9%	*Week 4*	0.21
	WL+C	3	13%	3	13%	2	9%	4	17%	*Week 8*	0.35
	Time	11	16%	6	9%	7	10%	7	10%	*Week 12*	0.35
Wake Up in the Middle of Night?	PLA	7	32%	8	36%	6	27%	7	32%	*Week 0*	0.87
	WL	8	35%	13	57%	10	43%	7	30%	*Week 4*	0.33
	WL+C	9	39%	9	39%	12	52%	11	48%	*Week 8*	0.23
	Time	24	35%	30	44%	28	41%	25	37%	*Week 12*	0.40
Have to Get up to Use Bathroom?	PLA	8	36%	8	36%	5	23%	9	41%	*Week 0*	0.56
	WL	10	43%	8	35%	6	26%	3	13%	*Week 4*	0.95
	WL+C	12	52%	9	39%	11	48%	11	48%	*Week 8*	0.15
	Time	30	44%	25	37%	22	32%	23	34%	*Week 12*	0.03
Cannot Breathe Comfortably?	PLA	0	0%	1	5%	0	0%	1	5%	*Week 0*	0.37
	WL	1	4%	1	4%	1	4%	0	0%	*Week 4*	0.59
	WL+C	0	0%	0	0%	0	0%	0	0%	*Week 8*	0.37
	Time	1	1%	2	3%	1	1%	1	1%	*Week 12*	0.35
Cough or Snore Badly?	PLA	2	9%	0	0%	0	0%	1	5%	*Week 0*	0.74
	WL	1	4%	5	22%	1	4%	0	0%	*Week 4*	0.02
	WL+C	1	4%	1	4%	0	0%	1	4%	*Week 8*	0.37
	Time	4	6%	6	9%	1	1%	2	3%	*Week 12*	0.59
Feel Too Cold?	PLA	1	5%	0	0%	2	9%	2	9%	*Week 0*	0.35
	WL	2	9%	1	4%	2	9%	3	13%	*Week 4*	0.07
	WL+C	4	17%	4	17%	3	13%	3	13%	*Week 8*	0.87
	Time	7	10%	5	7%	7	10%	8	12%	*Week 12*	0.89
Feel Too Hot?	PLA	1	5%	5	23%	2	9%	4	18%	*Week 0*	0.14
	WL	4	17%	3	13%	3	13%	6	26%	*Week 4*	0.36
	WL+C	6	26%	7	30%	9	39%	5	22%	*Week 8*	0.02
	Time	11	16%	15	22%	14	21%	15	22%	*Week 12*	0.81
Had Bad Dreams?	PLA	1	5%	1	5%	3	14%	1	5%	*Week 0*	0.59
	WL	1	4%	2	9%	2	9%	1	4%	*Week 4*	0.78
	WL+C	0	0%	1	4%	2	9%	2	9%	*Week 8*	0.82
	Time	2	3%	4	6%	7	10%	4	6%	*Week 12*	0.78
Have Pain?	PLA	2	9%	1	5%	1	5%	1	5%	*Week 0*	0.87
	WL	2	9%	1	4%	4	17%	2	9%	*Week 4*	0.44
	WL+C	3	13%	3	13%	1	4%	1	4%	*Week 8*	0.20
	Time	7	10%	5	7%	6	9%	4	6%	*Week 12*	0.78
Other Reasons?	PLA	5	23%	3	14%	4	18%	5	23%	*Week 0*	0.04
	WL	2	9%	3	13%	2	9%	1	4%	*Week 4*	0.85
	WL+C	0	0%	2	9%	1	4%	1	4%	*Week 8*	0.30
	Time	7	10%	8	12%	7	10%	7	10%	*Week 12*	0.07

Table 16.1 – Continued

Variable		Group	0 N	0 %	4 N	4 %	8 N	8 %	12 N	12 %	χ^2	
Quality of Sleep Rating?	*Very Good*	PLA	5	23%	6	27%	7	32%	6	27%	*Week 0*	0.39
		WL	6	26%	3	13%	7	30%	4	17%	*Week 4*	0.35
		WL+C	2	9%	1	4%	1	4%	2	9%	*Week 8*	0.16
		Time	13	19%	10	15%	15	22%	12	18%	*Week 12*	0.22
	Fairly Good	PLA	13	59%	15	68%	14	64%	13	59%		
		WL	15	65%	18	78%	14	61%	17	74%		
		WL+C	19	83%	19	83%	20	87%	15	65%		
		Time	47	69%	52	76%	48	71%	45	66%		
	Fairly Bad	PLA	4	18%	1	5%	1	5%	3	14%		
		WL	2	9%	2	9%	2	9%	1	4%		
		WL+C	2	9%	2	9%	2	9%	6	26%		
		Time	8	12%	5	7%	5	7%	10	15%		
	Very Bad	PLA	0	0%	0	0%	0	0%	0	0%		
		WL	0	0%	0	0%	0	0%	1	4%		
		WL+C	0	0%	1	4%	0	0%	0	0%		
		Time	0	0%	1	1%	0	0%	1	1%		
Enthusiasm to Get Things Done?	*No problem*	PLA	8	36%	15	68%	11	50%	12	55%	*Week 0*	0.43
		WL	13	57%	12	52%	11	48%	12	52%	*Week 4*	0.53
		WL+C	12	52%	12	52%	13	57%	13	57%	*Week 8*	0.43
		Time	33	49%	39	57%	35	51%	37	54%	*Week 12*	0.81
	Slight problem	PLA	10	45%	4	18%	9	41%	8	36%		
		WL	6	26%	9	39%	7	30%	9	39%		
		WL+C	5	22%	6	26%	8	35%	6	26%		
		Time	21	31%	19	28%	24	35%	23	34%		
	Somewhat of a problem	PLA	4	18%	3	14%	1	5%	2	9%		
		WL	4	17%	2	9%	5	22%	2	9%		
		WL+C	6	26%	4	17%	1	4%	4	17%		
		Time	14	21%	9	13%	7	10%	8	12%		
	Big problem	PLA	0	0%	0	0%	1	5%	0	0%		
		WL	0	0%	0	0%	0	0%	0	0%		
		WL+C	0	0%	1	4%	1	4%	0	0%		
		Time	0	0%	1	1%	2	3%	0	0%		
Frequency of snoring loudly?		PLA	4	18%	2	9%	2	9%	2	9%	*Week 0*	0.64
		WL	2	9%	4	17%	2	9%	4	17%	*Week 4*	0.71
		WL+C	3	13%	3	13%	1	4%	1	4%	*Week 8*	0.79
		Time	9	13%	9	13%	5	7%	7	10%	*Week 12*	0.34
Frequency of long pauses in your breathing?		PLA	0	0%	0	0%	0	0%	0	0%	*Week 0*	0.36
		WL	1	4%	1	4%	1	4%	0	0%	*Week 4*	0.37
		WL+C	2	9%	0	0%	0	0%	1	4%	*Week 8*	0.37
		Time	3	4%	1	1%	1	1%	1	1%	*Week 12*	0.37
Frequency of leg twitching while sleeping?		PLA	2	9%	3	14%	3	14%	3	14%	*Week 0*	1.00
		WL	2	9%	2	9%	2	9%	1	4%	*Week 4*	0.82
		WL+C	2	9%	2	9%	2	9%	2	9%	*Week 8*	0.82
		Time	6	9%	7	10%	7	10%	6	9%	*Week 12*	0.55
Frequency of disorientation or confusion during sleep?		PLA	0	0%	0	0%	0	0%	0	0%	*Week 0*	-
		WL	0	0%	0	0%	0	0%	0	0%	*Week 4*	-
		WL+C	0	0%	0	0%	0	0%	0	0%	*Week 8*	-
		Time	0	0%	0	0%	0	0%	0	0%	*Week 12*	-
Other restlessness while sleeping?		PLA	4	18%	4	18%	2	9%	4	18%	*Week 0*	0.52
		WL	2	9%	1	4%	1	4%	1	4%	*Week 4*	0.17
		WL+C	2	9%	1	4%	1	4%	0	0%	*Week 8*	0.74
		Time	8	12%	6	9%	4	6%	5	7%	*Week 12*	0.05

Data are presented as frequencies and percent N (N=68). Statistical significance is detailed from chi-squared analysis. Columns report the number of people whom responded and the percent of total number within each group. Time reports the total number of responders and the percent of total number of participants.

Table 17: Side Effects Frequency

			Rating of Symptom						
Symptom	**Weeks**	**Group**	**0**	**1**	**2**	**3**	**4**	**5**	χ^2
Dizziness	0	PLA	18	4	0	0	0	0	0.52
		WL	20	2	1	0	0	0	
		WL+C	21	1	1	0	0	0	
	4	PLA	19	3	0	0	0	0	0.69
		WL	20	3	0	0	0	0	
		WL+C	20	2	0	0	0	1	
	8	PLA	20	1	0	0	1	0	0.47
		WL	19	3	1	0	0	0	
		WL+C	21	1	0	0	0	1	
	12	PLA	19	2	1	0	0	0	0.75
		WL	20	2	0	0	1	0	
		WL+C	21	1	1	0	0	0	
Headache	0	PLA	13	7	2	0	0	0	0.22
		WL	19	3	1	0	0	0	
		WL+C	15	5	0	1	2	0	
	4	PLA	13	5	2	2	0	0	0.53
		WL	15	7	1	0	0	0	
		WL+C	14	6	1	0	1	1	
	8	PLA	14	6	0	1	1	0	0.77
		WL	17	5	1	0	0	0	
		WL+C	14	6	1	1	0	1	
	12	PLA	18	3	0	0	1	0	0.17
		WL	16	5	1	0	1	0	
		WL+C	15	4	0	4	0	0	
Tachycardia	0	PLA	20	2	0	0	0	0	0.24
		WL	21	1	0	1	0	0	
		WL+C	21	0	2	0	0	0	
	4	PLA	21	1	0	0	0	0	0.45
		WL	20	2	1	0	0	0	
		WL+C	17	2	1	2	0	1	
	8	PLA	22	0	0	0	0	0	0.07
		WL	21	2	0	0	0	0	
		WL+C	18	0	2	2	0	1	
	12	PLA	21	1	0	0	0	0	0.66
		WL	21	1	1	0	0	0	
		WL+C	19	1	2	0	0	1	
Heart Palpitations	0	PLA	20	2	0	0	0	0	0.39
		WL	22	1	0	0	0	0	
		WL+C	22	0	1	0	0	0	
	4	PLA	22	0	0	0	0	0	0.43
		WL	22	1	0	0	0	0	
		WL+C	21	0	0	1	1	0	
	8	PLA	22	0	0	0	0	0	0.43
		WL	22	1	0	0	0	0	
		WL+C	21	0	1	0	0	1	
	12	PLA	21	1	0	0	0	0	0.67
		WL	22	1	0	0	0	0	
		WL+C	20	1	1	0	0	1	

Table 17 – Continued

Symptom	Weeks	Group	Rating of Symptom 0	1	2	3	4	5	χ^2
Dyspnea	0	PLA	20	1	1	0	0	0	0.86
		WL	21	1	0	1	0	0	
		WL+C	19	2	1	1	0	0	
	4	PLA	20	2	0	0	0	0	0.24
		WL	20	1	2	0	0	0	
		WL+C	19	1	0	2	1	0	
	8	PLA	21	1	0	0	0	0	0.59
		WL	21	1	1	0	0	0	
		WL+C	19	2	0	1	0	1	
	12	PLA	22	0	0	0	0	0	0.53
		WL	22	0	1	0	0	0	
		WL+C	20	1	1	0	0	1	
Nervousness	0	PLA	16	4	1	0	1	0	0.37
		WL	18	1	2	2	0	0	
		WL+C	17	3	0	3	0	0	
	4	PLA	19	2	0	1	0	0	0.57
		WL	18	2	1	1	1	0	
		WL+C	21	0	0	2	0	0	
	8	PLA	17	3	2	0	0	0	0.78
		WL	17	4	1	0	1	0	
		WL+C	19	1	2	0	1	0	
	12	PLA	17	2	3	0	0	0	0.39
		WL	20	0	2	0	0	1	
		WL+C	19	0	3	1	0	0	
Blurred Vision	0	PLA	21	1	0	0	0	0	0.64
		WL	22	1	0	0	0	0	
		WL+C	20	2	0	1	0	0	
	4	PLA	20	2	0	0	0	0	0.55
		WL	20	2	1	0	0	0	
		WL+C	21	0	1	1	0	0	
	8	PLA	19	2	1	0	0	0	0.67
		WL	20	2	1	0	0	0	
		WL+C	21	0	1	1	0	0	
	12	PLA	21	1	0	0	0	0	0.33
		WL	21	0	2	0	0	0	
		WL+C	21	1	0	1	0	0	
Other	0	PLA	22	0	0	0	0	0	0.61
		WL	22	1	0	0	0	0	
		WL+C	22	1	0	0	0	0	
	4	PLA	22	0	0	0	0	0	0.40
		WL	22	1	0	0	0	0	
		WL+C	19	2	0	0	1	1	
	8	PLA	22	0	0	0	0	0	0.41
		WL	22	1	0	0	0	0	
		WL+C	22	0	0	0	1	0	
	12	PLA	22	0	0	0	0	0	0.13
		WL	23	0	0	0	0	0	
		WL+C	21	0	0	2	0	0	

Data are presented as frequencies. Statistical significance is detailed from chi-squared analysis. 1: minimal (1-2 per/wk); 2: slight (3-4 per/wk); 3: occasional (5-6 per/wk); 4: frequent (7-8 per/wk); 5: severe (9 < per/wk)

Table 18: Side Effects Severity

			Rating of Symptom						
Symptom	**Weeks**	**Group**	**0**	**1**	**2**	**3**	**4**	**5**	χ^2
Dizziness	0	PLA	19	2	0	1	0	0	0.66
		WL	20	2	1	0	0	0	
		WL+C	21	2	0	0	0	0	
	4	PLA	18	3	0	0	1	0	0.60
		WL	20	2	0	1	0	0	
		WL+C	20	2	0	0	0	1	
	8	PLA	21	0	0	0	1	0	0.29
		WL	19	3	0	1	0	0	
		WL+C	21	1	0	0	0	1	
	12	PLA	19	2	0	1	0	0	0.75
		WL	20	1	0	1	0	1	
		WL+C	21	2	0	0	0	0	
Headache	0	PLA	12	1	6	3	0	0	0.57
		WL	19	0	3	1	0	0	
		WL+C	15	1	4	3	0	0	
	4	PLA	14	1	4	3	0	0	0.21
		WL	15	6	1	1	0	0	
		WL+C	16	2	1	3	0	1	
	8	PLA	15	2	3	2	0	0	0.52
		WL	17	4	0	2	0	0	
		WL+C	16	1	2	3	0	1	
	12	PLA	18	3	0	1	0	0	0.47
		WL	18	2	0	1	1	1	
		WL+C	16	1	2	3	1	0	
Tachycardia	0	PLA	21	1	0	0	0	0	0.56
		WL	22	0	1	0	0	0	
		WL+C	22	1	0	0	0	0	
	4	PLA	21	1	0	0	0	0	0.34
		WL	22	1	0	0	0	0	
		WL+C	18	2	2	0	1	0	
	8	PLA	21	1	0	0	0	0	0.66
		WL	21	1	1	0	0	0	
		WL+C	19	1	2	1	0	0	
	12	PLA	21	1	0	0	0	0	0.40
		WL	20	2	1	0	0	0	
		WL+C	18	1	3	0	1	0	
Heart Palpitations	0	PLA	20	2	0	0	0	0	0.18
		WL	23	0	0	0	0	0	
		WL+C	22	0	1	0	0	0	
	4	PLA	21	1	0	0	0	0	0.41
		WL	22	0	1	0	0	0	
		WL+C	20	0	2	0	1	0	
	8	PLA	22	0	0	0	0	0	0.24
		WL	22	1	0	0	0	0	
		WL+C	20	0	2	1	0	0	
	12	PLA	21	1	0	0	0	0	0.52
		WL	23	0	0	0	0	0	
		WL+C	20	1	1	0	1	0	

Table 18 – Continued

			Rating of Symptom						
Symptom	**Weeks**	**Group**	**0**	**1**	**2**	**3**	**4**	**5**	χ^2
Dyspnea	0	PLA	20	2	0	0	0	0	0.41
		WL	22	0	1	0	0	0	
		WL+C	19	3	1	0	0	0	
	4	PLA	20	2	0	0	0	0	0.44
		WL	20	1	1	1	0	0	
		WL+C	20	0	2	0	1	0	
	8	PLA	21	1	0	0	0	0	0.61
		WL	21	1	1	0	0	0	
		WL+C	20	2	0	0	1	0	
	12	PLA	21	1	0	0	0	0	0.67
		WL	22	1	0	0	0	0	
		WL+C	20	1	1	1	0	0	
Nervousness	0	PLA	17	2	2	1	0	0	0.69
		WL	18	2	0	3	0	0	
		WL+C	17	3	2	1	0	0	
	4	PLA	19	0	3	0	0	0	0.66
		WL	18	1	2	2	0	0	
		WL+C	20	1	1	1	0	0	
	8	PLA	17	4	1	0	0	0	0.79
		WL	17	3	1	2	0	0	
		WL+C	18	2	1	1	1	0	
	12	PLA	17	2	2	1	0	0	0.26
		WL	20	2	0	0	0	1	
		WL+C	19	1	0	3	0	0	
Blurred Vision	0	PLA	21	1	0	0	0	0	0.55
		WL	22	0	1	0	0	0	
		WL+C	20	2	1	0	0	0	
	4	PLA	20	2	0	0	0	0	0.84
		WL	20	2	1	0	0	0	
		WL+C	21	1	1	0	0	0	
	8	PLA	19	2	1	0	0	0	0.73
		WL	20	3	0	0	0	0	
		WL+C	21	1	1	0	0	0	
	12	PLA	20	2	0	0	0	0	0.24
		WL	21	0	2	0	0	0	
		WL+C	21	1	0	1	0	0	
Other	0	PLA	22	0	0	0	0	0	-
		WL	23	0	0	0	0	0	
		WL+C	23	0	0	0	0	0	
	4	PLA	22	0	0	0	0	0	0.53
		WL	22	1	0	0	0	0	
		WL+C	20	1	1	0	0	1	
	8	PLA	22	0	0	0	0	0	0.41
		WL	22	0	1	0	0	0	
		WL+C	22	0	0	0	1	0	
	12	PLA	22	0	0	0	0	0	0.13
		WL	23	0	0	0	0	0	
		WL+C	21	0	0	2	0	0	

Data are presented as frequencies. Statistical significance is detailed from chi-squared analysis. 1: minimal; 2: slight; 3: moderate; 4: severe; 5: very severe

CHAPTER V

DISCUSSION AND CONCLUSIONS

Summary

Weight loss remains a goal for people globally in an effort to improve health and reduce risk associated with obesity and related comorbidities such as cardiovascular disease and type-2 diabetes mellitus. While diet and exercise modification are primary recommendations, dietary supplements such as fiber, appetite suppressors, lipolytic agents, and stimulants like caffeine are commonly used. As such, there is a constant search for alternatives like *Dichrostachys glomerata* (DG). Previous research has reported that DG supplementation (200-800 mg/d) for 8 weeks (2-months) led to significant reductions in weight and fat between 7-11 kg and 3-5%, respectively, without exercise or diet intervention. In comparison, the placebo interventions were reported to have lost <1 kg of body weight and <1% body fat. These data come from three trials performed by Kuate et al. and are the only studies, to date, that have tested DG in this manner. Of them, the lowest dose appeared to be the most effective, reporting weight loss of ~11 kg. However, the amount they administered is unclear seeing as the paper's abstract states 200 mg, twice a day (BID) but, the methods section implies only a single 200 mg/d dose. In addition, the aforementioned experiment sampled from a metabolic syndrome population.[3] The only other trial looked at a normoglycemic obese population and type-2 diabetic population with 800 mg/d (400mg BID), resulting in weight loss of ~7.5 and ~6 kg, respectively.[4,5] Consequently, further investigation is required to corroborate these findings.

The current study examined two multi-ingredient weight loss supplements containing DG, with and without caffeine [WL+C, WL], compared to a placebo (6g dextrose) over a 12-week, or 3-month, period. This double-blind trial ran with parallel groups and was randomized using a stratification method. Participants were evaluated for body weight/composition, anthropometry, clinical health markers, reported hunger, satiety, side effects, and sleep effects. The results of which showed statistically significant ($p<0.05$) decrease in FM from baseline at week 4 (-0.56±0.95 kg, $p=0.01$) and week 8 (-0.63±1.47 kg, $p=0.04$), for the non-caffeine group [WL], with a continued trend into week 12 (-0.71±1.47 kg, $p=0.08$). It is worth noting that FM exhibited a steady decline while body weight did not change. In line with this, supplement groups displayed parallel trends in FFM, gaining small amounts consistently through week 12 from baseline (WL 0.26±2 kg [p=0.5-0.9], WL+C 0.11±1.9 kg [p=0.7-0.8]), compared to the decline seen in placebo (-0.32±2 kg [p=0.4-0.6]). Moreover, BMC (g) showed little to no deviation or trend among treatment groups.

The results of the present study are in direct contrast to previous literature by Kuate et al., purporting significant weight loss over 8 weeks of DG supplementation and were the primary templates this study was modeled after. In 2011, Kuate et al. examined the effects of DG supplementation on normoglycemic and type-2 diabetic obese populations with 25 males and 72 females, age 25-65, in a double-blind, randomized, placebo-controlled fashion where both groups had 46 people split evenly into placebo or supplement for a total of 4 groups.[4] A 2013 follow-up to this experiment by the same group utilized an identical protocol except this time sampling from a metabolic syndrome

population involving 116 males and 202 females, age 24-58, split into either placebo or supplement groups, looking at an aqueous DG extract.[3] The amount of weight loss achieved in these trials far exceeds any observed in this present one, and in a shorter period. To elaborate, the first study[4] examined a similar population and sample size to ours, showing both supplement groups had lost around 6-7 kg of body weight compared to -1 kg in placebo, then the second study[3] resulted in loss of about 11 kg and the placebo lost <1 kg. Despite this, weight loss remained unaffected by DG in our current trial through 8 weeks and continuing as far as 12 weeks, with <0.5 kg decrease in weight at both time points. What's more, several of the other changes that accompanied the weight reduction in previous literature were not observed in this case. Generally, changes to BMI (-2 to -4 kg/m^2), waist and hip (-6 to -10, -3 to -9 cm) measurements, and body fat (-2 to -5%) paralleled the weight loss purported.[3,4] As opposed to the current DG outcomes for BMI (-0.12, -0.14 kg/m^2), waist (0.45, 1.52 cm) and hip (-0.25, -0.14 cm) at weeks 8 and 12, respectively, which are more comparable to that of the previous trials placebo results than their supplement group. The exception in this regard was the modest trend forming in reduction of fat mass as DG supplementation continued (-0.5, -0.6, -0.7 kg) through weeks 4, 8, and 12, respectively.

Blood pressure also showed little fluctuation with the current DG supplementation for 8 or 12 weeks, where systolic and diastolic pressure stayed within ±2 mmHg from baseline in all groups. Alternatively, the Kuate et al. trials reported comparable results with placebo but, DG saw significantly decreased blood pressure $\frac{SBP}{DBP}\frac{[-13 \text{ to } -24]}{[-10 \text{ to } -15]}$ mmHg. Similarly, the primary clinical health markers examined showed no significant changes by

week 8 or week 12, for our group respectively, including blood glucose (-0.1, -1.5 mg/dL), triglycerides (-5.3, 18.3 mg/dL), total cholesterol (-7.4, -6.7 mg/dL), LDL (12.8, -3.4 mg/dL), and HDL (-3.2, -4.8 mg/dL) and did not differ from placebo. However, the Kuate et al. trials all presented large reductions after 8 weeks that were also significantly different from placebo for blood glucose (-28.9 to -104.1 mg/dL), triglycerides (-55.4 to -105.1 mg/dL), total cholesterol (-43.1 to -96.8 mg/dL), and LDL (-50.2 to -84.8 mg/dL) with increased HDL (20.6 to 39.6 mg/dL).[3,4]

In their 2011 study, Kuate et al. had a diabetic group with an average baseline "fasting" glucose of around 200 mg/dL for placebo and DG, which is typically the expected value for the same population, 2 hours post-prandial. Even the "normoglycemic" group in the same study was closer to, even within the range of, prediabetes (100-125 mg/dL).[203] Their 2013 trial had similar levels, except this was by design. Never the less, these trials, especially in 2011, seem as though hyperglycemia could have played a potential role in causing a sort of hypohydrated state, and subsequently water retention in the form of intracellular water, allowing these parameters to improve as drastically as they did. Water retention would also explain the reported drop in body fat percent over 8 weeks as participants began to correct their fluid balance, possibly due to monitoring, considering the measurements were obtained using bioelectric impedance which is known to report higher fat percent with water retention and lower fat percent with dehydration.[204] Not to mention that it has been shown to be realistically possible and commonly done, to lose as much as 6% body mass in just 5 days, where nearly all of the weight was fluid yet, intracellular water remained unchanged.[205] Therefore, the notion of such a process

occurring over an 8-week span is more than feasible. By comparison, *Table 9* shows the fluid content and distribution, for this current trial, to have remained relatively consistent over the span of 12 weeks in all groups. Unfortunately, the hydration data is not reported for any of the previous trials, leaving no way to confirm or deny this theory but it is worth bearing in mind.

With regards the other supplements used in this investigation, ashwaganda was another primary nutrient of interest and one whose previous literature shows to be in line with some of the findings in our current study. Cooley et al. showed an average weight loss of around 2 kg as well as a decrease in BMI of about 0.75 kg/m^2 for 36 individuals ingesting 300 mg, BID with a multi-vitamin and naturopathic lifestyle encouragement spanning 12 weeks. This was weighed against a placebo control (-0.5 kg, -0.2 kg/m^2), otherwise similar group.[32] Then Raut et al. took eighteen apparently healthy volunteers (M 12; F 6, age: 20-27, 66.7±8.8 kg, BMI 24.3±2.7 kg/m^2) and described an increase in muscle force by 2-6 kg (handgrip, quadriceps, back-extensor) with no exercise intervention, an increasing trend in lean body mass (1.8 kg), decreasing trend in body fat (-2.3%), reduced total cholesterol (-16.3 mg/dL), and a trend in lowering LDL (-15.2 mg/dL), triglycerides (-7 mg/dL), and blood glucose (-4.6 mg/dL), after 30 days. This intervention used an increasing dose of 750 mg/d x10 days, 1,000 mg/d x 10 days, and 1,250 mg/d x 10 days, exhibiting no change in body weight. However, note that body composition was assessed via skinfold thickness and, with it being exploratory, there lacked a placebo control.[35]

Along the same lines, a few other supplements have been reported to affect resting metabolism such as capsaicinoids and caffeine. As such, we sought to measure resting energy expenditure by utilizing an indirect calorimeter metabolic cart. There were no differences between any groups in terms of resting energy expenditure (kcals per day). Yet, there appeared to be a trend forming wherein REE fluctuated lower then increased in WL (-28±201; -44±200; 55±213 kcal/d) and even more so in WL+C (58±205; 18±256; 111±220 kcal/d), at weeks 4, 8, and 12, respectively. In comparison, placebo looked to be on a downward trend after first increasing the number of kcals utilized at rest (162±277; 135±310; 92±284 kcal/d), from weeks 4, 8, and 12, respectively. Similar trends were seen for REE/kg in WL (-0.16±2.40; -0.49±2.35; 0.62±2.65 kcal/kg/d), WL+C (1.01±2.02; 0.59±2.61; 1.57±2.375 kcal/kg/d), and placebo (1.84±2.65; 1.38±2.75; 1.03±2.74 kcal//kg/d) from weeks 4, 8, and 12, respectively. Additionally, we observed supplement groups reported hunger severity to be generally less than their baseline with satiety being greater than baseline mostly in the non-caffeinated group, while placebo showed no changes but was consistently greater than other groups. As expected, there were no differences in diet characteristics or reported side effects. This was the expectation simply because there is hardly, if any literature suggesting the opposite.

The current results are seemingly in agreement with previous literature. For example, a systematic review performed by Whiting et al. in 2012 looked at 20 trials ranging from 1-135 mg/d, for 1 day 4 months, with samples sizes of 7-91. Of them, 13 studies showed increased energy expenditure of around 50 kcal/d, 7 reported increased lipid oxidation, and 5 reported decreased appetite and increased satiety.[11] A 2014

systematic review and meta-analysis by Whiting et al., concluded with 8 studies and 191 participants having reduced ad libitum energy intake averaging -74 kcal per meal when consuming capsaicin (0.2-33 mg) approximately 30 minutes before a meal, essentially reducing energy consumption.[10]

The non-caffeinated group, in the current trial, exhibited some slight sleep quality improvements in that they fell asleep between 5-6 minutes faster than when they started by weeks 8 and 12. In addition, they fell asleep a bit easier, with fewer interruptions such as waking to use the bathroom, in comparison to the caffeinated group that reported increased bathroom use. As well, the caffeine group reported to take longer to fall asleep than placebo at weeks 4 and 12 by approximately 18 and 8 minutes, respectively. These sleep quality results are supported by literature for both ashwaganda and theanine supplementation for help with sleep. Ashwaganda is traditionally used in ayurvedic medicine and puported within that literature to be a natural sleep aid.[35] Whereas theanine by itself has been shown, for example, by Lyon et al. to improve sleep quality in boys 8-12 years old diagnosed with ADHD, with administration of 400 mg/d.[121] Furthermore, a review by Juneja et al. reported relaxing effects with as little as a one-time dose of 50 mg. [116] For context, the current study's non-caffeine group ingested 100 mg of theanine daily. However, when theanine has been paired with caffeine, there is an opposing stimulating effect following administrations of 40-150 mg of caffeine paired with 9-250 mg of theanine.[105-109] Arguably, these outcomes could be the result of simply consuming caffeine, of which WL+C ingested around 350 mg/d, with no theanine.

Conclusions

Supplementation of a weight loss formula containing DG showed to have no significant effect on body weight using the current dose (300 mg/d). The addition of caffeine did not alter this outcome. However, supplement groups did show a trend in loss of FM with a subsequent reduction in BF percent, while the placebo group stayed relatively stable throughout the study. Even so, there were no differences between groups for either weight or body composition.

These trends in body composition are however in keeping with previous findings using one of the other primary nutrients of the current study, ashwaganda, where participants exhibited weight and body fat loss, as well as an increase in lean mass/muscular strength without exercise.[32,35] Clinical health markers however, showed no change, in contrast to the evidence of previous literature, primarily of DG and capsaicin, suggesting improvements in glucose and other markers related to obesity and metabolic syndrome, such as lipid profiles.[3-5,22,23] Other nutrients including capsaicin and caffeine, have shown to work either as primary driver or synergistically towards weight loss. Caffeine is commonly used in weight loss supplements as a way of increasing thermogenesis, energy expenditure, and fat oxidation.[6-9] In the same way, capsaicin is looked at for its' purported abilities to improve fat metabolism and as an appetite suppressant.[10-25] When capsaicin is coupled with caffeine they have shown to suppress hunger, increase feelings of satiety, and increase postprandial thermogenesis.[15,26] Ultimately, these factors could contribute to weight loss and its' continued maintenance. Our results would seem to agree with this literature, showing an increase in REE from

baseline. Supplement groups had increased REE from baseline with a greater improvement in the caffeinated group than the non-caffeinated group but, both groups more so than placebo.

While moderate changes ingesting 300 mg/d of DG with other nutrients promoted modest effects on body composition, it was nowhere near those purported previously. A consideration to be made is the dose of 300 mg/d may not have been sufficient to induce larger changes in weight loss, especially in a relatively healthy obese population and based on an unclear dose in previous literature. Currently, there are just three trials that tested DG in similarly to this study, as such the results of this investigation further highlight the need to put forth data that come from a group besides Kuate et al. In particular, because we produced results that are not in agreement with the previous literature, as well as extended supplementation by 4 weeks to no avail. Lastly, this trial was the first of this design with DG to measure body composition via DEXA scans, provide potentially important hydration data, as well as test in conjunction with caffeine ingestion.

In closing, further research is certainly required to determine an effective dose and subsequently paired with a diet and/or exercise intervention for functional assessment of the weight loss and metabolic aid potential. As well, the initial studies performed by Kuate et al. should be reproduced, taking into consideration the clinical populations that were examined, to confirm their results and tease out whether DG shows to be more effective in normal or clinical populations. Following that, similar testing could be done in different geographical regions, investigating how ubiquitous DG may or may not be in affecting people.

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APPENDIX A

Nonprotein Respiratory Quotient Calculation

$$E = G + \frac{GCO_2 - CO_2 \cdot RQ}{FO_2 \cdot RQ - FCO_2} \cdot F$$

$Oxidation$: (1g glucose)

$G = 3.8683$kcal/g
$GO_2 = 0.7455$ L of O_2 (STPD)/g
$GCO_2 = 0.7426$ L of CO_2 (STPD)/g

$Oxidation$: (1g Fatty Acids)

$F = 9.746$kcal/g
$FO_2 = 2.0092$ L of O_2 (STPD)/g
$FCO_2 = 1.4136$ L of CO_2 (STPD)/g

E (energy produced) = (1g of glucose)+([x]g fatty acids)

$$E = 3.8683 + \frac{0.7426 - 0.7455 \cdot RQ}{2.0092 \cdot RQ - 1.4136} \cdot 97460$$

$$\%\ \text{glucose} = \frac{3.8683}{E} \cdot 100 \qquad \%\ \text{fatty acids} = 100 - \%\ \text{glucose}$$

APPENDIX B

EDUCATION
& HUMAN DEVELOPMENT
TEXAS A&M UNIVERSITY

Want to lose weight?

Men and Women Needed for a Weight Loss Study

Researchers in the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University are recruiting approximately 150 apparently healthy, overweight to moderately obese (BMI = 25 – 34.9), recreationally active males and females between the ages of 30 and 45 to participate in a study. The study will examine a weight loss formula with and without common stimulants. Eligible participants will receive $200 for completing the study. Five total visits throughout approximately a 12 to 15 week period will be required.

For more information call:

Exercise & Sport Nutrition Laboratory (ESNL)
Department of Health & Kinesiology (HLKN)
1700 Research Parkway, Suite #2500
675 John Kimbrough Blvd, Suite #206
E-mail Ryan Sowinski
Rjs370@email.tamu.edu

IRB NUMBER: IRB2016-0829FX
IRB APPROVAL DATE: 12/21/2016
IRB EXPIRATION DATE: 12/01/2017

APPENDIX C

Texas A&M University: Exercise & Sport Nutrition Laboratory
Trial: An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk - Entrance Criteria

Phone Script:
"*Exercise and Sport Nutrition Lab, this is [name] how may I help you? If you are interested in the study titled An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Risk, I am going to ask you a series of questions."*

Entrance Criteria:

Age:

1. Are you between the ages of 30 & 45? (they must be 45 when they sign the consent, they may turn 46 during the study)

Yes – Possible FAM No – Screen Failure

Exercise History:

1. Are you apparently healthy?

Yes – Possible FAM No – Screen Failure

2. Are you moderately active and participate in low intensity recreational activity at least 3 to 4 d/wk?

Yes – Possible FAM No – Screen Failure

BMI (kg/m2):

1. Do you have a BMI between 25.0 and 34.9?

Yes – Possible FAM No – Screen Failure

Height (Inches)	Body Weight (Pounds)																					
58	91	95	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167	172	177	181	186	191
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173	178	183	188	193	198
60	97	102	107	112	118	123	128	133	138	143	148	153	158	164	169	174	179	184	189	194	199	204
61	100	106	111	116	121	127	132	137	143	148	153	158	164	169	174	180	185	190	195	201	206	211
62	104	109	115	120	125	131	136	142	147	153	158	164	169	175	180	186	191	196	202	207	213	218
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	192	197	203	208	214	220	225
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	198	203	209	215	221	227	233
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234	240
66	117	124	130	136	142	148	155	161	167	173	179	185	192	198	204	210	216	223	229	235	241	247
67	121	127	134	140	147	153	159	166	172	178	185	191	198	204	210	217	223	229	236	242	248	255
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	217	223	230	236	243	249	256	263
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	237	243	250	257	264	270
70	132	139	146	153	160	167	174	181	188	195	202	209	216	223	230	236	243	250	257	264	271	278
71	136	143	150	157	165	172	179	186	193	200	207	215	222	229	236	243	250	258	265	272	279	286
72	140	147	155	162	169	177	184	191	199	206	213	221	228	235	243	250	258	265	272	280	287	294
73	144	151	159	166	174	182	189	197	204	212	219	227	234	242	250	257	265	272	280	287	295	303
74	148	155	163	171	179	187	194	202	210	218	225	233	241	249	256	264	272	280	288	295	303	311
75	152	160	168	176	184	192	200	208	216	224	232	240	247	255	263	271	279	287	295	303	311	319
76	156	164	172	180	189	197	205	213	221	230	238	246	254	262	271	279	287	295	303	31		328
77	160	168	177	185	194	202	210	219	227	236	244	252	261	269	278	286	295	303	311	32		337

Exclusion Criteria:

1. Have you experienced a recent history of weight change (+/- 10 lbs. within 3 months)?

Yes – Screen Failure No – Possible FAM

2. Do you have any uncontrolled metabolic or cardiovascular disorders including; heart disease, hypertension, arrhythmias, diabetes, hypogonadism, hepatorenal, musculoskeletal, autoimmune, neurological disease or thyroid disease, or known electrolyte abnormalities?

Yes – Screen Failure No – Possible FAM

3. Are you currently taking medications or prescribed medications for less than six months? (birth control is allowed)?

Yes – Screen Failure No – Possible FAM

4. Are you taking any dietary supplements for thyroid, hyperlipidemia, hypoglycemia, or weight loss (e.g., ephedra or thermogenic compounds, etc.) or have you within the past three months?

Yes – Screen Failure No – Possible FAM

5. Are you pregnant or nursing or plan to become pregnant during the next month?

Yes – Screen Failure No – Possible FAM

6. Do you have an intolerance to caffeine and/or other natural stimulants?

Yes – Screen Failure No – Possible FAM

Summary:

If the potential participant meets all conditions for a possible FAM, please schedule them for a familiarization.

APPENDIX D

TEXAS A&M UNIVERSITY HUMAN RESEARCH PROTECTION PROGRAM

INFORMED CONSENT DOCUMENT

Project Title: **An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk**

You are invited to take part in a research study being conducted by Dr. Richard Kreider, a researcher from Texas A&M University and funded by Woodbolt International. The information in this form is provided to help you decide whether or not to take part. If you decide to take part in the study, you will be asked to sign this consent form. If you decide you do not want to participate, there will be no penalty to you, and you will not lose any benefits you normally would have. You may choose to withdraw from the study at any time without penalty. NOTE: If you are employed then it is your responsibility to work with your employer regarding work leave for participation in this study if during work hours.

Principle Investigator:
Richard B. Kreider, PhD, FACSM, FISSN, FACN
Texas A&M University, Department of Health & Kinesiology
Telephone: 979-845-1333; Email: rbkreider@tamu.edu

Why Is This Study Being Done?
The purpose of this study is to examine a new weight loss formula with and without common stimulants.

Why Am I Being Asked To Be In This Study?
You are being asked to be in this study because you are an apparently healthy, recreationally active male or female between the ages of 30 and 45 with a Body Mass Index (BMI) between 25 and 34.9. You will need to be moderately active and participate in three to four days of low intensity recreational activity per week. You will not be allowed to participate if you; have a recent history of weight change (± 10 lb. within 3 months), have any uncontrolled metabolic or cardiovascular disorders, including heart disease, hypertension, arrhythmias, diabetes, hypogonadism, hepatorenal, musculoskeletal, autoimmune, neurological disease or thyroid disease, or known electrolyte abnormalities; are currently taking or prescribed medications (birth control is allowed) for less than six months, have taken any dietary supplements for thyroid, hyperlipidemia, hypoglycemia or weight loss (e.g., ephedra or thermogenic compounds, etc.) within three months before the start of the study, are pregnant or were pregnant or lactating within the past year or have an interest in becoming pregnant during the study; have an intolerance to caffeine and/or other natural stimulants, or do not meet the average goal step count. The only exception to these will be if you have a medical condition or history that your personal physician feels is controlled and therefore would not be a limitation for you to participate in the study. In which case your physician will have to complete a Physician Clearance form for you to return. If you do not qualify for this study we will keep your contact information (phone number and/or e-mail) and contact you at a later date for potential entry into a similar study unless you object.

How Many People Will Be Asked To Be In This Study?
Approximately 150 people (participants) will be invited to participate in this study locally.

What Are the Alternatives to being in this study?
The alternative to being in the study is not to participate.

What Will I Be Asked To Do In This Study?

You will be asked to refrain from exercise and alcohol 48 hours prior to each testing session/visit nor eat or drink calorie containing foods/drinks 12 hours before each testing session/visit. Your participation in this study will last approximately 12 - 15 weeks and include five visits (visit 1 ~ 1 hour, visits 2-5 ~ 2 hours). We will ask you to donate a blood sample up to five times throughout the study and complete four body composition assessments. These visits are detailed below and in Table 1.

Visit 1 – Familiarization

This visit will last approximately one hour. During this visit we will explain the details of the study and ask you to sign a consent form and help complete a general screening form. We will complete a general physical that may include measurement of blood to determine if you can participate in the study. We may ask you to donate about 5 ml (about 1 teaspoon) of blood from a vein in your arm. Next we will measure body weight, body height and calculate BMI. We will then introduce you to the food log and provide dietary recall instructions. Then we will give you an activity tracker and ask you to wear it for five consecutive days (3 weekdays and 2 weekend days) and return it on your baseline testing session. Depending on when you start during the week you may choose Wednesday through Sunday or Saturday through Wednesday. Finally we will schedule your baseline visit.

Visit 2 – Baseline (T2)

This visit will last approximately 2 hours. We will first collect your activity tracker and figure your average daily step count. If you meet the average goal step count for this study we will continue with the baseline testing session. If you do not you will be removed from the study. First we will review your food log and ask you to complete a physical activity questionnaire, an eating satisfaction survey, a sleep index, a radiation exposure questionnaire and a side effects inventory. Next we will take a blood sample. Then we will measure your body weight, waist circumference and hip circumference and calculate your BMI. We will then measure your body water, body composition, heart rate and blood pressure followed by your resting energy expenditure (REE). Finally we will randomize you into either 1.) weight loss formula group with caffeine; 2.) weight loss formula group without caffeine; or 3.) placebo group (6 g dextrose). The formula tables are listed below. We will ask you to take your supplements in pill form twice a day. Once capsule in the morning between 7:00 a.m. and 9:00 a.m. and one capsule in the afternoon between 2:00 p.m. and 4:00 p.m. We will count your remaining pills at the upcoming visits to ensure your compliance and give you a full bottle at each visit (minus the final visit). Finally we will schedule your next visit.

Visit 3 – T3

This visit will last approximately 2 hours and include the same tests as the baseline visit.

Visit 4 – T4

This visit will last approximately 2 hours and include the same tests as the baseline visit.

Visit 5 – T5

This visit will last approximately 2 hours and include the same tests as the baseline visit. We will also ask you to come in approximately a week prior to pick up an activity tracker and wear it one final time for five consecutive days (3 weekdays and 2 weekend days).

Table 1 – Protocol Overview

Familiarization (T1)	T2 (Day 0)		T3 (Week 4/Day 28) Testing Visit 3	T4 (Week 8/Day 56) Testing Visit 4	T5 (Week 12/Day 84)	
Visit 1	Step Counter Assessment Run-In ~ 1 week prior	Baseline Testing Visit 2			Step Counter Assessment ~ 1 week prior	End Point Testing Visit 5
Phone Screening Informed Consent Body Weight/ Height/BMI Physical Exam Medical Clearance (if necessary) Introduction to Food Logs and Dietary Recall Distribute Activity Tracker and Schedule Testing Refrain from exercise & alcohol 48 hrs. prior to each testing session & calorie containing food & drink 12 hrs. prior to each testing session 1 – weight loss formula with caffeine 2 – weight loss formula without caffeine 3 – placebo (6 g dextrose)	Step Counter Assessment for 5 Days	Collect Activity Tracker Goal not met – exclude from study Goal met - proceed 4 Day Food Record PA Questionnaire Eating Survey Sleep Index Radiation Exposure Questionnaire Side Effects Inventory 12 Hour Fasting Blood Sample Body Weight BMI Waist/Hip HR/BP Body Water Body Composition REE Instructions for supplementation (randomized and counterbalanced manner)	Same as Baseline Testing (minus the Activity Tracker collection)	Same as Baseline Testing (minus the Activity Tracker collection)	Step Counter Assessment for 5 Days	Same as Baseline Testing

Study Formula

Stimulant Formula

AM (Between 7-9 a.m.)	
Dietary Ingredient	**Ingredient Input (mg/dose)**
XR Caffeine (77% Caffeine)	150
Sensoril	125
Caffeine Anhydrous 98.5%	100
Capsimax™ Capsicum Extract 4% Capsaicinoids	25
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	250
Magnesium Stearate	14
Total Quantity	**784**

PM (Between 2-4 p.m.)	
Dietary Ingredient	**Ingredient Input (mg/dose)**
DygloFit™ Dichrostachys glomerata extract	300
Caffeine Anhydrous 98.5%	150
Capsimax™ Capsicum Extract 4% Capsaicinoids	25
Clubmoss Ext 1% Huperzine	10
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	230
Magnesium Stearate	15
Total Quantity	**850**

Non-Stimulant Formula

AM (Between 7-9 a.m.)	
Dietary Ingredient	**Ingredient Input (mg/dose)**
Sensoril® Ashwaganda (Withania somnifera)	250
Bioperine	5
Capsimax® Cayenne (Capsicum annuum) fruit extract (4% Capsaicinoids)	25
Rhodiola rosea extract	60
	0
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	250
Magnesium Stearate	14
Total Quantity	**724**

PM (Between 2-4 p.m.)	
Dietary Ingredient	**Ingredient Input (mg/dose)**
DygloFit™ Dichrostachys glomerata extract	300
Capsimax® Cayenne (Capsicum annuum) fruit extract (4% Capsaicinoids)	25
L-Theanine	100
Toothed clubmoss (Huperzia serrata) aerial parts extract (1% Huperzine A)	5
Bacopa monneri extract	50
Other Ingredients	
Capsule, Gelatin, Size 00, White/White	120
Microcrystalline Cellulose 102	230
Magnesium Stearate	15
Total Quantity	**845**

You may be removed from the study by the investigator for these reasons:

- You do not show up for your scheduled testing sessions/visits and the investigators are unable to contact you to reschedule
- You do not meet the average goal step count
- You do not follow your assigned supplemental protocol
- You do not complete and turn in all questionnaires

_____ I give my permission for my records to be accessed for use in this research study.

_____ I do not give my permission for my records to be accessed for use in this research study.

Are There Any Risks To Me?
The things that you will be doing are greater than risks than you would come across in everyday life. Although the researchers have tried to avoid risks, you may feel that some questions/procedures that are asked of you will be stressful or upsetting. You do not have to answer anything you do not want. You will be exposed to a low level of radiation four times during the body composition exams, which is similar to the amount of natural background radiation you would receive in one month while living in College Station Texas. In addition, a very low level of electrical current will be passed through your body using a bioelectrical impedance analyzer four times. This analyzer is commercially available and has been used in the health care/fitness industry as a means to assess body composition and body water for over 20 years. The use of the body composition scanner and bioelectrical impedance analyzer have been shown to be safe methods of assessing body composition and total body water and are approved by the FDA. You may donate approximately 5 ml (about 1 teaspoon) of blood during the initial familiarization/screening visit and then approximately 20 ml (about 4 teaspoons) of blood four additional times throughout the entire study. The procedures may cause a small amount of pain when the needle is inserted into the vein as well as some bleeding and bruising. You may experience some dizziness and/or faint if you are unaccustomed to having blood drawn. However, only a trained phlebotomist will be performing blood sampling. If you are or were to become pregnant, the particular treatment or study procedure might involve risks to the embryo or fetus, which are currently unknown. You may also experience an upset stomach, GI distress and jitteriness due to the supplement.

Are There Any Benefits To Me?
The direct benefit to you by being in this study is to know more about your health and fitness status from the tests to be performed.

Will There Be Any Costs To Me?
If you drive you may have to pay approximately $5 each time you make a study visit depending on parking availability at our building.

Will I Be Paid To Be In This Study?
You will receive a total of $200 ($25 for the familiarization and baseline testing session and $50 for the remaining three testing sessions) in one check at the end of the study. Payment will occur after finishing all testing sessions and after all study materials (questionnaires, etc.) have been turned in to the study staff. You will be paid on a prorated basis if you are unable to complete the entire study.

Will I Have To Pay Anything If I Get Hurt In This Study?
If you suffer any injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment and professional services will be available to you, just as they are to the community in general. You should report any injury to Dr. Richard Kreider at 979-845-1333. You will not give up any of your legal rights by signing this consent form.

Side effects (injury) can happen in any research study. These effects may not be your fault or the fault of the researcher involved. Known side effects have been described in the "Are there any risks to me?" section of this consent form. However, side effects that are not currently known may happen and require care. In the event you experience side effects, particularly "unusual or adverse effects" you will be referred to or given the option of speaking with the Principle Investigator, Dr. Richard Kreider, the ESNL Research Nurse, Liz Martinez, the ESNL Protocol Director/Laboratory Research Associate, Mr.

Chris Rasmussen and/or the ESNL Supervising Physician Dr. J.P. Bramhall. If you are uncomfortable with these options, you are encouraged to discuss these side effects with your personal physician. You do not give up any of your legal rights by signing this form.

Will Information From This Study Be Kept Private?
The records of this study will be kept private. No identifiers linking you to this study will be included in any sort of report that might be published. Research records will be stored securely and only Exercise & Sport Nutrition Laboratory staff will have access to the records.

Information about you will be stored in locked file cabinets in an ID card swipe controlled laboratory. Computer files will be protected with a password. This consent form will be filed securely in an official area.

People who have access to your information include the Principal Investigator and research study personnel. Representatives of regulatory agencies such as the Office of Human Research Protections (OHRP) and entities such as the Texas A&M University Human Research Protection Program may access your records to make sure the study is being run correctly and that information is collected properly.

The agency that is funding this study (Woodbolt International) and the institution(s) where study procedures are being performed (Texas A&M University) may also see your information. However, any information that is sent to them will be coded with a number so that they cannot tell who you are. Representatives from these entities can see information that has your name on it if they come to the study site to view records. If there are any reports about this study, your name will not be in them.

Information about you and related to this study will be kept confidential to the extent permitted or required by law.

Incidental Findings: The tests in this study are for specific research and are not optimized to find medical abnormalities. The investigators for this study may not be trained to perform medical diagnosis. However, the investigator may notice a finding that appears to be abnormal, which might be detected during the imaging or during retrospective review of the data. When this occurs, a physician will be consulted as to whether the finding merits further investigation, in which case the investigator will contact you (and your primary care physician) and inform you of the finding. The decision as to whether to proceed with further examination of treatment lies solely with you and your physician.

Who may I Contact for More Information?
You may contact the Principal Investigator, Dr. Richard Kreider, PhD, to tell him about a concern or complaint about this research at 979-845-1333 or rbkreider@tamu.edu. You may also contact the Protocol Director/Laboratory Research Associate, Mr. Chris Rasmussen at 979-458-1741 or crasmussen@tamu.edu.

For questions about your rights as a research participant, to provide input regarding research, or if you have questions, complaints, or concerns about the research, you may call the Texas A&M University Human Research Protection Program (HRPP) by phone at 1-979-458-4067, toll free at 1-855-795-8636, or by email at irb@tamu.edu. The informed consent form and all study materials should include the IRB number, approval date, and expiration date. Please contact the HRPP if they do not.

What if I Change My Mind About Participating?
Your participation in this research is voluntary, and you have the choice whether or not to be in this research study. You may decide to not begin or to stop participating at any time. If you choose not to be in this study or stop being in the study, there will be no effect on your academic standing as a student, medical care, employment, evaluation, relationship with Texas A&M University, etc. Any new information discovered about the research will be provided to you. This information could affect your willingness to continue your participation.

STATEMENT OF CONSENT
I agree to be in this study and know that I am not giving up any legal rights by signing this form. The procedures, risks, and benefits have been explained to me, and my questions have been answered. I know that new information about this research study will be provided to me as it becomes available and that the researcher will tell me if I must be removed from the study. I can ask more questions if I want and I can still receive services if I stop participating in this study. A copy of this entire consent form will be given to me.

Participant's Signature	Date
Printed Name	Date

INVESTIGATOR'S AFFIDAVIT:
Either I have or my agent has carefully explained to the participant the nature of the above project. I hereby certify that to the best of my knowledge the person who signed this consent form was informed of the nature, demands, benefits and risks involved in his/her participation.

Signature of Presenter	Date
Printed Name	Date

APPENDIX E

General Screening Form

Study:_____ IRB: _____

Texas A&M, College Station, TX

Subject Initials [ ]

Consent Date [ ] [ ] [ ] (mm dd yyyy)

Screening Date [ ] [ ] [ ] (mm dd yyyy)

Visit: SCREENING

Name: _____

Address: _____

Phone #: _____

E-mail: _____

Local PCP: _____ ☐ None

_____

Demographics

Visit: SCREENING

Sex: ☐ M ☐ F

DOB: ☐☐ mm ☐☐ dd ☐☐☐☐ yyyy Age at enrollment: _____ y

Race: *(Mark all which apply)*

- ☐ White
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Asian
- ☐ American Indian/Alaska Native
- ☐ Unknown

Ethnicity: *(Mark only 1)*

- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino
- ☐ Unknown

Visit: SCREENING

Medications:

Nutritional Supplements:

Medical History:

Surgical History:

Exercise/Training History:

Current Exercise/Training Program:

Allergies and drug reactions:

Smoking: Duration: _____ PPD x _____ Yrs
Former smoker: when stopped: _____
Duration: _____ PPD x _____ Yrs

EtOH: _____

Vital signs:

HR: ____ m

BP: ____ / ____ mmHg

Anthropometry:
Height: ____ . ____ cm Weight: ____ . ____ kg BMI: ____ . ____ kg/m2
____ . ____ in ____ . ____ lb

Visit: SCREENING

ROS:	fever chills sweats wtΔ fatigue appetite sleep
Skin:	itching rash sores susp. moles/lesions- healing recentΔ
Head:	dizzy fainting HA/LOC trauma
Eyes:	correction Δvision-double tearing itching/redness
Ears:	Δhearing ringing earache vertigo/tinnitus
Nose:	epistaxis rhinorrhea allergies
Mouth/Throat:	bleeding gums sore mouth/throat swollen neck
CV:	angina palpitations DOE orthopnea/PND edema
Pulm:	SOB wheeze cough hemoptysis TB
Hematologic:	bruise /bleed easily transfusion hx
GI:	dysphagia N / V abd pain GERD hematochezia jaundice
GU:	freq urgency hesitancy dys- hematuria incont UTI's stones
Genital:	testicular masses hernias
Endocrine:	polyuria polydipsia skin/hair ? thyroid hx
Vascular:	claudication DVT hx
MSK:	jt pain stiffness arthritis gout
Neuro:	numbness weakness/atrophy seizure/tremor
Psych:	depression anxiety recent memoryΔ
Female:	regular dysmenorrhea pregnancies menopause
Breast:	skinΔ lumps pain discharge

PE:	Gen: Well
Skin:	cap refill: no rash lesions:
Head:	no trauma no bruising no masses
Eyes:	PERRLA EOMI no ptosis sclera clear
Ears:	good acuity TM: nl reflex/intact
Nose:	nl
Mouth/Throat:	nl/pink, moist mucous membranes no lesions
Neurological:	Alert & oriented×3, nl MS via conversation
Cranial Nerves:	II - XII intact/nl
Motor:	5/5 UE/LE's bil
Sensation:	intact LT UE/LE's
DTRs:	symmetric/nl biceps knee ankle
Gait/Station:	nl
Neck:	no LAD no masses no bruits no JVD supple stiff
Chest:	CTA bil equal expansion
Extremities:	no C/C/E Major jts: no swelling full ROM
Heart:	Reg no M/R/G
Pulses Bil:	PT / DP: 2+
Abdomen:	soft, NT/ND BS + no masses / organomegaly

Assessment: _____

Blood Draw: ☐ Y ☒ N _____

Blood draw performed by: N/A

Lab Results Reviewed: ☐ Y ☒ N

Eligible based on General Health and Physical Exam: ☐ Y ☐ N

_____ Date: ____ ____ ____

Signature of staff member performing exam mm dd yyyy

APPENDIX F

Texas A&M
UNIVERSITY

Dear Provider: One of your patient's would like to participate in a study titled "An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk" that is being conducted by the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University. In order to do so, he/she must meet the selection criteria described below and/or have approval from his/her personal physician to participate in the study. The assessments to be performed are listed below. Please check the test/tests you **do not** feel comfortable having your patient complete (if any). In addition please staple a copy of your letterhead to this form to verify that it has been reviewed.

_____Fasting blood

_____Fasting resting energy expenditure (REE)

_____Bone densitometry (DXA)

_____Bioelectrical Impedance Analysis (BIA)

Details about these specific tests are included below and in the attached participant consent form. If you feel he/she meets the entrance criteria and/or any existing medical condition that he/she may have is under control and **would not** be a limitation for them to participate in the study, please sign the medical clearance below.

Selection Criteria
Approximately 150 recreationally active (3-4 d/wk) males and females classified as overweight to class I obese (BMI – 25.0 – 34.9) between the ages of 30 and 45 will participate in a supplementation protocol for approximately 12 to 15 weeks. I understand that in order to participate in this study, a trained individual will examine potential participants to determine whether they qualify to participate.

Participants **will not** be allowed to participate in this study if they:
1. have recent history of weight change (±10 lb within 3 months),
2. have any *uncontrolled* metabolic or cardiovascular disorders including; heart disease, hypertension, arrhythmias, diabetes, hypogonadism, hepatorenal, musculoskeletal, autoimmune, neurological disease or thyroid disease, or known electrolyte abnormalities,
3. are currently taking medications or prescribed medications for less than six months (birth control is allowed),
4. have taken any dietary supplements for thyroid, hyperlipidemia, hypoglycemia, or weight loss (e.g., ephedra or thermogenic compounds, etc.) within three months before the start of the study,
5. are pregnant or were pregnant or lactating within the past year or have an interest in becoming pregnant during the study,
6. have an intolerance to caffeine and/or other natural stimulants.

The only exception to these selection criteria will be if the prospective participant has a medical condition or history that the participant's personal physician feels is controlled and therefore would not be a limitation for them to participate in the study.

Medical Clearance

I medically clear _____ to participate as a participant in this study.

Name _____ Date _____

Signature _____

Exercise & Sport Nutrition Lab
Department of Health & Kinesiology
Texas A&M University
TAMU 4253 · College Station, TX 77843-4253 · P (979) 458-1743 · F (979) 845-0837
http://hlknweb.tamu.edu

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Texas A&M
UNIVERSITY

Blood Samples. Participants will fast overnight for twelve hours and then donate approximately 1 teaspoon (5 milliliters) of fasting blood once and 4 teaspoons (20 milliliters) of fasting blood four times throughout the duration of the 12 week study. Blood samples will be obtained using standard phlebotomy procedures using standard sterile venipuncture of an antecubital vein by laboratory technician's trained in phlebotomy in compliance with guidelines established by the Texas Department of Health and Human Services. The phlebotomists and lab technicians will wear personal protective clothing (gloves, lab coats, etc.) when handling blood samples. Participants will be seated in a phlebotomy chair. Their arm will be cleaned with a sterile alcohol wipe and sterile gauze. A standard rubber tourniquet will then be placed on the brachium. An antecubital vein will be palpated and then a sterile needle attached to a plastic vacutainer holder will be inserted into the vein using standard procedures. Approximately two serum separation vacutainer tubes (red tops) and approximately one EDTA vacutainer tube (purple top) will be inserted into the vacutainer holder for blood collection in succession using multiple sample phlebotomy techniques. Once samples are obtained, the vacutainer holder and needle will be removed. The needle will be discarded as hazardous waste in a plastic sharps container. The site of the blood draw will then be cleaned with a sterile alcohol wipe and gauze and a sterile Band-Aid will be placed on the site. The blood collection tubes will be labeled and placed in a test tube rack for later analysis.

Resting Energy Expenditure Assessment. Resting energy expenditure assessments will be completed according to standard protocols using the Parvo Medics TrueOne 2400 Metabolic Measurement System. This will involve the participants lying down on an exam table, having a light blanket placed over them to keep warm and inserting ear plugs in their ears to reduce distractions. A see through metabolic canopy will then be placed over their neck and head so that metabolic measurements can be obtained. The participant will lie motionless without going to sleep for approximately 30 minutes. Metabolic measurements will then be obtained to determine resting oxygen uptake and energy expenditure.

Body Composition Assessments (BIA & DXA). Participants will undergo body composition tests in the ESNL. Prior to each assessment, height will be measured using standard anthropometry and total body weight will be measured using a calibrated electronic scale with a precision of +/-0.02 kg. Total body water will then be estimated using an Impedimed DF50 bioelectrical impedance analyzer which measures bio-resistance of water and body tissues based on a minute low energy, high frequency current (500 micro-amps at a frequency of 50 kHz) transmitted through the body. This analyzer is commercially available and has been used in the health care/fitness industry as a means to assess body composition and body water for over 20 years. The use of this device has been approved by the Food and Drug Administration (FDA) to assess total body water and the current to be used has been deemed safe. This is measured through four electrodes placed on the body: the electrodes on the foot are to be placed across the dorsum of the foot at the heads of the metatarsals. The other electrode on the foot is to be placed on the dorsum of the foot at the level of the subtalar (ankle) joint or crease. The other two electrodes are to be placed on the dorsum of the hand at the level of the heads of the metacarpals and the other at the crease of the wrist joint (over the carpal bones). Participants will lie on a table in the supine position and electrodes will be connected to the analyzer. After they are connected, age, gender, weight, height, and activity level are entered into the unit by the technician. After the unit has measured the resistance, which takes approximately 30 seconds, the unit then calculates total body water and body water percent.

Body composition/bone density will then be determined using a calibrated Hologic Discovery W dual-energy x-ray absorptiometry (DXA) by qualified personnel under the supervision of Richard B. Kreider, PhD, MX. The DXA body composition test will involve having the participant lie down on their back in a standardized position in a pair of shorts/t-shirt or a gown. A low dose of radiation will then scan their entire body for approximately six (6) minutes. The DXA segments regions of the body (right arm, left arm, trunk, right leg, and left leg) into three compartments for determination of fat, soft tissue (muscle), and bone mass. Radiation exposure from DXA for the whole body scan is approximately 1.5mR per scan. This is similar to the amount of natural background radiation a person would receive in one month while living in College Station, TX. The maximal permissible x-ray dose for non-occupational exposure is 500 mR per year. Total radiation dose will be less than 5mR for the entire study. Since women of child bearing age may serve as participants in this study, each participant will complete a questionnaire related to their menstrual cycle timing, sexual activity, use of birth control pills, and desire to become pregnant.

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Texas A&M University: Exercise & Sport Nutrition Laboratory
Trial: An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk

Radiation Exposure Questionnaire for Women of Child Bearing Age

Radiation exposure may affect fetal development. Although the DXA test will only expose you to a small amount of radiation (1.5mR per scan), you should be aware that there is a possibility that if you become pregnant during the course of the study that the x-ray exposure may be harmful to the fetus. Therefore, it is ideal to conduct x-ray tests within 10-14 days of the start of a female's menstrual cycle if the she is of child bearing age, sexually active, and/or is not taking birth control pills. The following questionnaire must be completed so that we know when it is an appropriate time to conduct the DXA body composition tests. Please be assured that this information will be kept confidential within the limits permitted by law.

Current Age? _____
Age of first period? _____
Date of last period? _____
Normal length of menstrual cycle? _____
Do you use birth control pills? _____
Are you pregnant or have a desire for pregnancy? _____

Note: If you happen to get pregnant during the course of this study, you must notify research assistants so that appropriate precautions can be made.

I confirm that I have completed this questionnaire honestly and agree to notify researchers within the ESNL of any change in the length of my menstrual cycle and/or pregnancy status.

_____ _____
Name Date

_____ _____
Staff Signature Date

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APPENDIX H

Texas A&M University: Exercise & Sport Nutrition Laboratory
Trial: An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk

Demographics ESNL Staff Initials: _____

Name: _____ Testing Session: _____ Group: _____
Date: _____ D.O.B.: _____ Age: _____
Activity Tracker: _____ (5 day average)

Paper Work ESNL Staff Initials: _____

Informed Consent/General Screening Form/Questionnaires:

HLKN Informed consent: _____ Short Sleep: _____
Radiation consent: _____ Side Effects: _____
Food Log: _____ Eating Satisfaction: _____
IPAQ: _____ General Screening Form: _____

Physiological Parameters: ESNL Staff Initials: _____

Height:	_____ in.	Resting H.R.:	_____ bpm.
Weight:	_____ lb.	Resting B.P.:	_____/_____ mmHg
BMI:	_____ kg/m²	BIA:	_____
REE (30 m.):	_____ #1 or #2	FFM (kg)	_____ _____
Time:	_____ am	FM (kg)	_____ _____
Last Meal:	_____ am/pm	TBW (L)	_____ _____
Hrs. Fasted:	_____ hr.	ICW (L)	_____ _____
Lab:	_____ (2) SST Tubes/ (1) EDTA Tube	ECW (L)	_____ _____
Waist:	_____ in.	Handheld BIA:	_____ #1 or #2
Hip:	_____ in.	DXA:	_____

Updated 11/21/2016

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Exercise and Sport Nutrition Laboratory

An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk - Food Record

Name: _____ Day: 1 2 3 4 (Circle One)

Instructions:

1) Record everything that you eat for 3 weekdays AND 1 weekend day
2) Precisely record the food item (brand if applicable), preparation method, and TOTAL quantity consumed
3) Break down mixed dishes or recipes by listing their component parts
4) For dairy and meat products, indicate fat level (i.e. low fat, extra lean, 2%, etc.)

FOOD ITEM	PREPARATION METHOD (i.e. baked, fried, grilled, etc.)	QUANTITY							
		gm	mL	cups	T or tsp.	oz.	Pieces	Sm, Med, Lg	Other
MEAL 1:									
MEAL 2:									
MEAL 3:									
MEAL 4:									

APPENDIX J

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (August 2002)

SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ
The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ
Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation
Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ
International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information
More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective*. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day**

   _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

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4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

APPENDIX K

Texas A&M University: Exercise & Sport Nutrition Laboratory
Trial: An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk

Eating Satisfaction Survey

Name: _____ Group: _____ Date: _____

INSTRUCTIONS

Circle the number or dot between numbers that best indicates the degree you have felt the following symptoms during the last week:

Appetite

None Low Moderate High Severe
0.....1.....2.....3.....4.....5.....6.....7.....8.....9.....10

Hunger

None Low Moderate High Severe
0.....1.....2.....3.....4.....5.....6.....7.....8.....9.....10

Satisfaction from Food

None Low Moderate High Severe
0.....1.....2.....3.....4.....5.....6.....7.....8.....9.....10

Feeling of Fullness

None Low Moderate High Severe
0.....1.....2.....3.....4.....5.....6.....7.....8.....9.....10

Amount of Energy

None Low Moderate High Severe
0.....1.....2.....3.....4.....5.....6.....7.....8.....9.....10

Overall Quality of Diet

None Low Moderate High Severe
0.....1.....2.....3.....4.....5.....6.....7.....8.....9.....10

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APPENDIX L

Name: _____ Group: _____ Date: _____

SLEEP QUALITY INDEX INSTRUCTIONS

The following questions relate to your usual sleep habits during the past 48 hrs

Please answer *all* questions.

1. During the past 48 hrs, what time have you usually gone to bed at night?

BED TIME _____

2. During the past 48 hrs, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

3. During the past 48 hrs, what time have you usually gotten up in the morning?

GETTING UP TIME _____

4. During the past 48 hrs, how many hours of actual sleep did you get at night? (This may be different from the number of hours you spent in bed.)

HOURS OF SLEEP PER NIGHT _____

FOR EACH OF THE REMAINING QUESTIONS.

5. During the past 48 hrs, have you had trouble sleeping because you **(Check All That Apply)**

__ Cannot get to sleep within 30 minutes

__ Wake up in the middle of the night or early morning

__ Have to get up to use the bathroom

__ Cannot breathe comfortably

__ Cough or snore loudly

__ Feel too cold

__ Feel too hot

__ Had bad dreams

__ Have pain

__ Other reason(s), please describe

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6. During the past 48 hrs, how would you rate your sleep quality overall?

__ Very good

__ Fairly good

__ Fairly bad

__ Very bad _____

7. During the past 48 hrs, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

__ No problem at all

__ Only a very slight problem

__ Somewhat of a problem

__ A very big problem

8. Do you have a bed partner or room mate?

__ No bed partner or room mate

__ Partner/room mate in other room

__ Partner in same room, but not same bed

__ Partner in same bed

9. If you have a roommate or bed partner, ask them how often in the past 48 hrs you have had . . .

__ Loud snoring

__ Long pauses between breaths while asleep

__ Legs twitching or jerking while you sleep

__ Episodes of disorientation or confusion during sleep

10. Other restlessness while you sleep; please describe

Texas A&M University: Exercise & Sport Nutrition Laboratory

Trial: An Examination of a Novel Weight Loss Formula on Anthropometry and Indices of Cardiovascular Disease Risk – Weekly Follow-Up Assessment

Name: _____ Group: _____ Date: _____

Week	1	2	3	4	5	6	7	8	9	10	11	12
Are you taking your supplements?												
Rate the frequency of the following symptoms according to the scale where: 0 = none 1 = minimal (1-2 per/wk) 2 = slight (3-4 per/wk) 3 = occasional (5-6 per/wk) 4 = frequent (7-8 per/wk) 5 = severe (9 or more per/wk)												
Dizziness?												
Headache?												
Fast or racing heart rate?												
Heart skipping/palpitations?												
Shortness of breath?												
Nervousness?												
Blurred Vision?												
Any other adverse events?												
Rate the severity of the following symptoms according to the scale where: 0 = none 1 = minimal 2 = slight 3 = moderate 4 = severe 5 = very severe												
Dizziness?												
Fast or racing heart rate?												
Headache?												
Heart skipping/palpitations?												
Shortness of breath?												
Nervousness?												
Blurred Vision?												
Any other adverse events?												

PLEASE REMEMBER TO REPORT WEEKLY TO THE RESEARCH ASSISTANTS @ the ESNL

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